

A METHOD FOR ISOLATING A POLYNUCLEOTIDE OF INTEREST FROM THE GENOME OF A MYCOBACTERIUM USING A BAC-BASED DNA LIBRARY. APPLICATION TO THE DETECTION OF MYCOBACTERIA.

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I. Background of the invention

The present invention pertains to a method for isolating a polynucleotide of interest that is present in the genome of a mycobacterium strain and/or is expressed by said mycobacterium strain and that is absent or altered in the
10 genome of a different mycobacterium strain and/or is not expressed in said different mycobacterium strain, said method comprising the use of at least one clone belonging to a genomic DNA library of a given mycobacterium strain, said DNA library being cloned in a bacterial artificial chromosome (BAC). The invention concerns also polynucleotides identified by the above method, as well
15 as detection methods for mycobacteria, particularly *Mycobacterium tuberculosis*, and kits using said polynucleotides as primers or probes. Finally, the invention deals with BAC-based mycobacterium DNA libraries used in the method according to the invention and particularly BAC-based *Mycobacterium tuberculosis* and *Mycobacterium bovis* BCG DNA libraries.

20 Radical measures are required to prevent the grim predictions of the World Health Organisation for the evolution of the global tuberculosis epidemic in the next century becoming a tragic reality. The powerful combination of genomics and bioinformatics is providing a wealth of information about the etiologic agent, *Mycobacterium tuberculosis*, that will facilitate the conception and development
25 of new therapies. The start point for genome sequencing was the integrated map of the 4.4 Mb circular chromosome of the widely-used, virulent reference strain, *M. tuberculosis* H37Rv and appropriate cosmids were subjected to systematic shotgun sequence analysis at the Sanger Centre.

Cosmid clones (Balasubramanian et al., 1996; Pavelka et al., 1996) have
30 played a crucial role in the *M. tuberculosis* H37Rv genome sequencing project. However, problems such as under-representation of certain regions of the chromosome, unstable inserts and the relatively small insert size complicated the production of a comprehensive set of canonical cosmids representing the entire genome.

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II. Summary of the invention

In order to avoid the numerous technical constraints encountered in the state of the art, as described hereabove, when using genomic mycobacterial DNA libraries constructed in cosmid clones, the inventors have attempted to realize
5 genomic mycobacterial DNA libraries in an alternative type of vectors, namely Bacterial Artificial Chromosome (BAC) vectors.

The success of this approach depended on whether the resulting BAC clones could maintain large mycobacterial DNA inserts. There are various reports describing the successful construction of a BAC library for eucaryotic organisms
10 (Cai et al., 1995; Kim et al., 1996; Misumi et al., 1997; Woo et al., 1994; Zimmer et al., 1997) where inserts up to 725 kb (Zimmer et al., 1997) were cloned and stably maintained in the *E. coli* host strain.

Here, it is shown that, surprisingly, the BAC system can also be used for mycobacterial DNA, as 70% of the clones contained inserts in the size of 25 to
15 104 kb.

This is the first time that bacterial, and specifically mycobacterial, DNA is cloned in such BAC vectors.

In an attempt to obtain complete coverage of the genome with a minimal overlapping set of clones, a Bacterial Artificial Chromosome (BAC) library of *M. tuberculosis* was constructed, using the vector pBeloBAC11 (Kim et al., 1996)
20 which combines a simple phenotypic screen for recombinant clones with the stable propagation of large inserts (Shizuya et al., 1992). The BAC cloning system is based on the *E. coli* F-factor, whose replication is strictly controlled and thus ensures stable maintenance of large constructs (Willems et al., 1987).
25 BACs have been widely used for cloning of DNA from various eucaryotic species (Cai et al., 1995; Kim et al., 1996; Misumi et al., 1997; Woo et al., 1994; Zimmer et al., 1997). In contrast, to our knowledge this report describes the first attempt to use the BAC system for cloning bacterial DNA.

A central advantage of the BAC cloning system over cosmid vectors used
30 in prior art is that the F-plasmid is present in only one or a maximum of two copies per cell, reducing the potential for recombination between DNA fragments and, more importantly, avoiding the lethal overexpression of cloned bacterial genes. However, the presence of the BAC as just a single copy means that plasmid DNA has to be extracted from a large volume of culture to obtain

sufficient DNA for sequencing and it is described here in the examples a simplified protocol to achieve this.

Further, the stability and fidelity of maintenance of the clones in the BAC library represent ideal characteristics for the identification of genomic differences possibly responsible for phenotypic variations in different mycobacterial species.

As it will be shown herein, BACs can be allied with conventional hybridization techniques for refined analyses of genomes and transcriptional activity from different mycobacterial species.

Having established a reliable procedure to screen for genomic polymorphisms, it is now possible to conduct these comparisons on a more systematic basis than in prior art using representative BACs throughout the chromosome and genomic DNA from a variety of mycobacterial species.

As another approach to display genomic polymorphisms, the inventors have also started to use selected H37Rv BACs for "molecular combing" experiments in combination with fluorescent *in situ* hybridization (Bensimon et al., 1994; Michalet et al., 1997). With such techniques the one skilled in the art is enabled to explore the genome of mycobacteria in general and of *M. tuberculosis* in particular for further polymorphic regions.

The availability of BAC-based genomic mycobacterial DNA libraries constructed by the inventors have allowed them to design methods and means both useful to identify genomic regions of interest of pathogenic mycobacteria, such as *Mycobacterium tuberculosis*, that have no counterpart in the corresponding non-pathogenic strains, such as *Mycobacterium bovis* BCG, and useful to detect the presence of polynucleotides belonging to a specific mycobacterium strain in a biological sample.

By a biological sample according to the present invention, it is notably intended a biological fluid, such as plasma, blood, urine or saliva, or a tissue, such as a biopsy.

Thus, a first object of the invention consists of a method for isolating a polynucleotide of interest that is present in the genome of a mycobacterium strain and/or is expressed by said mycobacterium strain and that is absent or altered in the genome of a different mycobacterium strain and/or is not expressed in said different mycobacterium strain, said method comprising the use of at least one clone belonging to a genomic DNA library of a given mycobacterium strain, said DNA library being cloned in a bacterial artificial chromosome (BAC).

The invention is also directed to a polynucleotide of interest that has been isolated according to the above method and in particular a polynucleotide containing one or several Open Reading Frames (ORFs), for example ORFs encoding either a polypeptide involved in the pathogenicity of a mycobacterium strain or ORFs encoding Polymorphic Glycine Rich Sequences (PGRS).

Such polynucleotides of interest may serve as probes or primers in order to detect the presence of a specific mycobacterium strain in a biological sample or to detect the expression of specific genes in a particular mycobacterial strain of interest.

The BAC-based genomic mycobacterial DNA libraries generated by the present inventors are also part of the invention, as well as each of the recombinant BAC clones and the DNA insert contained in each of said recombinant BAC clones.

The invention also pertains to methods and kits for detecting a specific mycobacterium in a biological sample using either at least one recombinant BAC clone or at least one polynucleotide according to the invention, as well as to methods and kits to detect the expression of one or several specific genes of a given mycobacterial strain present in a biological sample.

III. Brief description of the Figures.

In order to better understand the present invention, reference will be made to the appended figures which depicted specific embodiments to which the present invention is in no case limited in scope with.

Figures 1A and 1B : PCR-screening for unique BAC clones with specific primers for 2 selected genomic regions of the H37Rv chromosome, using 21 pools representing 2016 BACs (Figure 1A) and sets of 20 subpools from selected positive pools (Figure 1B).

Figure 2 : Pulsed-field gel electrophoresis gel of *DraI*-cleaved BAC clones used for estimating the insert sizes of BACs.

Figure 3 : Minimal overlapping BAC map of *M. tuberculosis* H37Rv superimposed on the integrated physical and genetic map established by Philipp et al. (18). Y- and I- numbers show pYUB328 (2) and pYUB412 (16) cosmids which were shotgun sequenced during the H37Rv genome sequencing project. Y-cosmids marked with * were shown in the integrated physical and genetic map

(18). Rv numbers show the position of representative BAC clones relative to sequenced Y- and I- clones. Squared Rv numbers show BACs which were shotgun sequenced at the Sanger Centre.

5 **Figures 4A and 4B** : Ethidium bromide stained gel (Figure 4A) and corresponding Southern blot (Figure 4B) of *Eco*RI and *Pvu*II digested Rv58 DNA hybridized with ³²P labeled genomic DNA preparations from *M. tuberculosis* H37Rv, *M. bovis* ATCC 19210 and *M. bovis* BCG Pasteur.

Figure 5 : Organisation of the ORFs in the 12.7 kb genomic region present in *M. tuberculosis* H37Rv but not present in *M. bovis* ATCC 19210 and *M. bovis* BCG Pasteur. Arrows show the direction of transcription of the putative genes. Positions of *Eco*RI and *Pvu*II restriction sites are shown. Vertical dashes represent stop codons. The 11 ORFs correspond to the ORFs MTCY277.28 to MTCY277.38 / accession number Z79701 -EMBL Nucleotide Sequence Data Library. The junction sequences flanking the polymorphic region are shown.

15 **Figure 6** : Variation in the C-terminal part of a PE-PGRS open reading frame in *M. tuberculosis* strain H37Rv relative to *M. bovis* BCG strain Pasteur.

The numbers on the right side of the Figure denote the position of the end nucleotides, taking as the reference the *M. tuberculosis* genome.

Figure 7 : Polynucleotide sequence next to the HindIII cloning site in the BAC vector pBeloBAC11 (Kim et al., 1996) used to clone the inserts of the BAC-based myobacterial genomic DNA library according to the invention.

NotI : location of the NotI restriction sites.

Primer T7-BAC1 : nucleotide region recognized by the T7-BAC1 primer shown in Table 1.

25 T7 promoter : location of the T7 promoter region on the pBeloBac11 vector.

Primer T7-Belo2 : nucleotide region recognized by the T7-Belo2 primer shown in Table 1.

Hind III : the HindIII cloning site used to clone the genomic inserts in the pBeloBAC11 vector.

30 SP6-Mid primer : nucleotide region recognized by the SP6 Mid primer shown in Table 1.

SP6-BAC1 primer : nucleotide region recognized by the SP6 BAC1 primer shown in Table 1.

SP6 promoter : location of the SP6 promoter region on the pBeloBac11 vector.

IV. Detailed description of the preferred embodiments.

As already mentioned hereinbefore, the present invention is directed to a method for isolating a polynucleotide of interest that is present in the genome of a mycobacterium strain and/or is expressed by said mycobacterium strain and that is absent or altered in the genome of a different mycobacterium strain and/or is not expressed in said different mycobacterium strain, said method comprising the use of at least one clone belonging to a genomic DNA library of a given mycobacterium strain, said DNA library being cloned in a bacterial artificial chromosome (BAC) type vector.

For this purpose, the inventors have constructed several BAC-based mycobacterial genomic DNA libraries that may be used in order to perform the above described method.

Because it is the first time that mycobacterial genomic DNA has been successfully cloned in BAC type vectors, and because these DNA libraries are then novel and nonobvious, an object of the present invention consists in a mycobacterial genomic DNA library cloned in such a BAC type vector.

As an illustrative example, a BAC-based DNA library of *Mycobacterium tuberculosis* has been realized. Forty-seven cosmids chosen from the integrated map of the 4.4 Mb circular chromosome (Philipp et al., 1996a) were shotgun-sequenced during the initial phase of the H37Rv genome sequence project. The sequences of these clones were used as landmarks in the construction of a minimally overlapping BAC map. Comparison of the sequence data from the termini of 420 BAC clones allowed us to establish a minimal overlapping BAC map and to fill in the existing gaps between the sequence of cosmids. As well as using the BAC library for genomic mapping and sequencing, we also tested the system in comparative genomic experiments in order to uncover differences between two closely related mycobacterial species. As shown in a previous study (Philipp et al., 1996b), *M. tuberculosis*, *M. bovis* and *M. bovis* BCG, specifically BCG Pasteur strain, exhibit a high level of global genomic conservation, but certain polymorphic regions were also detected. Therefore, it was of great interest to find a reliable, easy and rapid way to exactly localize polymorphic regions in mycobacterial genomes using selected BAC clones. This approach was validated by determining the exact size and location of the polymorphisms in the genomic region of *DraI* fragment Z4 (Philipp et al., 1996b), taking advantage of the availability of an appropriate BAC clone covering the polymorphic region and

the H37Rv genome sequence data. This region is located approximately 1.7 Mb from the origin of replication.

The Bacterial Artificial Chromosome (BAC) cloning system is capable of stably propagating large, complex DNA inserts in *Escherichia coli*. As part of the *Mycobacterium tuberculosis* H37Rv genome sequencing project, a BAC library was constructed in the pBeloBAC11 vector and used for genome mapping, confirmation of sequence assembly, and sequencing. The library contains about 5000 BAC clones, with inserts ranging in size from 25 to 104 kb, representing theoretically a 70 fold coverage of the *M. tuberculosis* genome (4.4 Mb). A total of 840 sequences from the T7 and SP6 termini of 420 BACs were determined and compared to those of a partial genomic database. These sequences showed excellent correlation between the estimated sizes and positions of the BAC clones and the sizes and positions of previously sequenced cosmids and the resulting contigs. Many BAC clones represent linking clones between sequenced cosmids, allowing full coverage of the H37Rv chromosome, and they are now being shotgun-sequenced in the framework of the H37Rv sequencing project. Also, no chimeric, deleted or rearranged BAC clones were detected, which was of major importance for the correct mapping and assembly of the H37Rv sequence. The minimal overlapping set contains 68 unique BAC clones and spans the whole H37Rv chromosome with the exception of a single gap of ~ 150 kb. As a post-genomic application, the canonical BAC set was used in a comparative study to reveal chromosomal polymorphisms between *M. tuberculosis*, *M. bovis* and *M. bovis* BCG Pasteur, and a novel 12.7 kb segment present in *M. tuberculosis* but absent from *M. bovis* and *M. bovis* BCG was characterized. This region contains a set of genes whose products show low similarity to proteins involved in polysaccharide biosynthesis. The H37Rv BAC library therefore provides the one skilled in the art with a powerful tool both for the generation and confirmation of sequence data as well as for comparative genomics and a plurality of post-genomic applications.

The above described BAC-based *Mycobacterium tuberculosis* genomic DNA library is part of the present invention and has been deposited in the Collection Nationale de Cultures de Microorganismes (CNCM) on November 19, 1997 under the accession number I-1945.

Another BAC-based DNA library has been constructed with the genomic DNA of *Mycobacterium bovis* BCG, Pasteur strain, and said DNA library has

been deposited in the Collection Nationale de Cultures de Microorganismes (CNCM) on XX XX, 1998 under the accession number I-XXXX.

Thus, as a specific embodiment of the above described method for isolating a polynucleotide of interest said method makes use of at least one BAC-based DNA library that has been constructed from the genomic DNA of
5 *Mycobacterium tuberculosis*, more specifically of the H37Rv strain and particularly of the DNA library deposited in the accession number I-1945.

In another specific embodiment of the above described method for isolating a polynucleotide of interest said method makes use of at least one BAC-based DNA library has been constructed from the genomic DNA of
10 *Mycobacterium bovis* BCG, more specifically of the Pasteur strain and particularly of the DNA library deposited in the accession number I-XXXX.

In more details, the method according to the invention for isolating a polynucleotide of interest may comprise the following steps :

- 15 a) isolating at least one polynucleotide contained in a clone of a BAC-based DNA library of mycobacterial origin;
- b) isolating :
 - at least one genomic or cDNA polynucleotide from a mycobacterium, said mycobacterium belonging to a strain different from the strain used to construct the BAC-based DNA library of step a); or alternatively
 - 20 - at least one polynucleotide contained in a clone of a BAC-based DNA library prepared from the genome of a mycobacterium that is different from the mycobacterium used to construct the BAC-based DNA library of step a);
- c) hybridizing the at least one polynucleotide of step a) to the at least one
25 polynucleotide of step b);
- d) selecting the at least one polynucleotide of step a) that has not formed a hybrid complex with the at least one polynucleotide of step b);
- e) characterizing the selected polynucleotide.

Following the above procedure, the at least one polynucleotide of step a)
30 may be prepared as follows :

- 1) digesting at least one recombinant BAC clone by an appropriate restriction endonuclease in order to isolate the polynucleotide insert of interest from the vector genetic material;
- 2) optionally amplifying the resulting polynucleotide insert;

3) optionally digesting the polynucleotide insert of step 1) or step 2) with at least one restriction endonuclease.

The above method of the invention allows the one skilled in the art to perform comparative genomics between different strains or species of mycobacteria cells, for example between pathogenic strains or species and their non pathogenic strains or species counterparts, as it is the illustrative case for the genomic comparison between *Mycobacterium tuberculosis* and *Mycobacterium bovis* BCG that is described herein in the examples.

Restriction digests of a given clone of a BAC library according to the invention may be blotted to membranes, and then probed with radiolabeled DNA from another strain or another species of mycobacteria, allowing the one skilled in the art to identify, characterize and isolate a polynucleotide of interest that may be involved in important metabolic and/or physiological pathways of the mycobacterium under testing, such as a polynucleotide functionally involved in the pathogenicity of said given mycobacteria for its host organism.

More specifically, the inventors have shown in Example 6 that when restriction digests of a given clone of the BAC library identified by the CNCM accession number I-1945 are blotted to membranes and then probed with radiolabeled total genomic DNA from, for example, *Mycobacterium bovis* BCG Pasteur, it is observed that restriction fragments that fail to hybridize with the *M. bovis* BCG Pasteur DNA are absent from its genome, hence identifying polymorphic regions between *M. bovis* BCG Pasteur and *M. tuberculosis* H37Rv.

Thus, a further object of the present invention consists in a polynucleotide of interest that has been isolated according to the method described herein before.

In Example 6, a polynucleotide of approximately 12.7 kilobases has been isolated that is present in the genome of *M. tuberculosis* but is absent of the genome of *M. bovis* BCG. This polynucleotide of interest contains 11 ORFs that may be involved in polysaccharide biosynthesis. In particular, two of said ORFs are of particular interest, namely ORF6 (MTCY277.33; Rv1511) that encodes a protein that shares significant homology with bacterial GDP-D-mannose dehydratases, whereas the protein encoded by ORF7 (MTCY277.34; Rv1512) shares significant homology with a nucleotide sugar epimerase. As polysaccharide is a major constituent of the mycobacterial cell wall, these deleted genes may cause the cell wall of *M. bovis* BCG to differ from that of *M. tuberculosis*, a fact that may have important consequences for both the immune

response to *M. bovis* BCG and virulence. Detection of such a polysaccharide is of diagnostic interest and possibly useful in the design of tuberculosis vaccines.

Consequently, the polynucleotide of interest obtained following the method according to the invention may contain at least one ORF, said ORF
5 preferably encoding all or part of a polypeptide involved in an important
metabolical and/or physiological pathway of the mycobacteria under testing, and
more specifically all or part of a polypeptide that is involved in the pathogenicity
of the mycobacteria under testing, such as for example *Mycobacterium*
tuberculosis, and more generally mycobacteria belonging to the *Mycobacterium*
10 *tuberculosis* complex.

The *Mycobacterium tuberculosis* complex has its usual meaning, i.e. the complex of mycobacteria causing tuberculosis which are *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum*, *Mycobacterium microti* and the vaccine strain *Mycobacterium bovis* BCG.

15 An illustrative polynucleotide of interest according to the present invention comprises all or part of the polynucleotide of approximately 12.7 kilobases that is present in the genome of *M. tuberculosis* but is absent from the genome of *M. bovis* BCG disclosed hereinbefore. This polynucleotide is contained in clone Rv58 of the BAC DNA library I-1945.

20 Generally, the invention also pertains to a purified polynucleotide comprising the DNA insert contained in a recombinant BAC vector belonging to a BAC-based mycobacterial genomic DNA library, such as for example the I-1945 BAC DNA library.

Advantageously, such a polynucleotide has been identified according to
25 the method of the invention.

Such a polynucleotide of interest may be used as a probe or a primer useful for specifically detecting a given mycobacterium of interest, such as *Mycobacterium tuberculosis* or *Mycobacterium bovis* BCG.

More specifically, the invention then deals with a purified polynucleotide
30 useful as probe or a primer comprising all or part of the nucleotide sequence SEQ ID N°1.

The location, on the *Mycobacterium tuberculosis* chromosome, of the above polynucleotide of sequence SEQ ID N°1 has now been ascribed to begin, at its 5' end at nucleotide at position nt 1696015 and to end, at its 3' end, at
35 nucleotide at position nt 1708746.

For diagnostic purposes, this 12.7 kb deletion should allow a rapid PCR screening of tubercle isolates to identify whether they are bovine or human strains. The primers listed in Table 1 are flanking the deleted region and give a 722 bp amplicon in *M. bovis* or *M. bovis* BCG strains, but a fragment of 13,453 bp in *M. tuberculosis* that is practically impossible to amplify under the same PCR conditions. More importantly, assuming that some of the gene products from this region represent proteins with antigenic properties, it could be possible to develop a test that can reliably distinguish between the immune response induced by vaccination with *M. bovis* BCG vaccine strains and infection with *M. tuberculosis* or that the products (e.g. polysaccharides) are specific immunogens.

The invention also provides for a purified polynucleotide useful as a probe or as a primer, said polynucleotide being chosen in the following group of polynucleotides :

- a) a polynucleotide comprising at least 8 consecutive nucleotides of the sequence SEQ ID N°1;
- b) a polynucleotide whose sequence is fully complementary to the sequence of the polynucleotide defined in a);
- c) a polynucleotide that hybridizes under stringent hybridization conditions with the polynucleotide defined in a) or with the polynucleotide defined in b).

For the purpose of defining a polynucleotide or oligonucleotide hybridizing under stringent hybridization conditions, such as above, it is intended a polynucleotide that hybridizes with a reference polynucleotide under the following hybridization conditions.

The hybridization step is realized at 65°C in the presence of 6 x SSC buffer, 5 x Denhardt's solution, 0,5% SDS and 100µg/ml of salmon sperm DNA.

For technical information, 1 x SSC corresponds to 0.15 M NaCl and 0.05M sodium citrate; 1 x Denhardt's solution corresponds to 0.02% Ficoll, 0.02% polyvinylpyrrolidone and 0.02% bovine serum albumin.

The hybridization step is followed by four washing steps :

- two washings during 5 min, preferably at 65°C in a 2 x SSC and 0.1%SDS buffer,
- one washing during 30 min, preferably at 65°C in a 2 x SSC and 0.1% SDS buffer,
- one washing during 10 min, preferably at 65°C in a 0.1 x SSC and 0.1%SDS buffer.

A first illustrative useful polynucleotide that is included in the polynucleotide of sequence SEQ ID N°1 is the polynucleotide of sequence SEQ ID N°2 that corresponds to the Sp6 end-sequence of SEQ ID N°1.

5 A second illustrative useful polynucleotide that is included in the polynucleotide of sequence SEQ ID N°1 is the polynucleotide of sequence SEQ ID N°3 that corresponds to the T7 end-sequence of SEQ ID N°1, located on the opposite strand.

10 The polynucleotide of sequence SEQ ID N°1 contains 11 ORFs, the respective locations of which, taking into account the orientation of each ORF on the chromosome, on the sequence of the *Mycobacterium tuberculosis* chromosome, is given hereafter :

- The location of ORF1 is comprised between nucleotide at position nt 1695944 and nucleotide at position nt1696441.
 - The location of ORF2 is comprised between nucleotide at position nt 1696728 and nucleotide at position nt1697420.
 - The location of ORF3 is comprised between nucleotide at position nt 1698096 and nucleotide at position nt1699892. ORF3 probably encodes a protein having the characteristics of a membrane protein.
 - The location of ORF4 is comprised between nucleotide at position nt 1700210 and nucleotide at position nt1701088.
 - The location of ORF5 is comprised between nucleotide at position nt 1701293 and nucleotide at position nt1702588. ORF5 encodes a protein having the characteristics of a membrane protein.
 - The location of ORF6 is comprised between nucleotide at position nt 1703072 and nucleotide at position nt1704091. ORF6 encodes a protein having the characteristics of a GDP-D-mannose dehydratase.
 - The location of ORF7 is comprised between nucleotide at position nt 1704091 and nucleotide at position nt1705056. ORF7 encodes a protein having the characteristics of a nucleotide sugar epimerase involved in colanic acid biosynthesis.
 - The location of ORF8 is comprised between nucleotide at position nt 1705056 and nucleotide at position nt1705784.
 - The location of ORF9 is comprised between nucleotide at position nt 1705808 and nucleotide at position nt1706593. ORF9 encodes a protein having the characteristics of colanic acid biosynthesis glycosyl transferase.
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- The location of ORF10 is comprised between nucleotide at position nt 1706631 and nucleotide at position nt1707524.
- The location of ORF11 is comprised between nucleotide at position nt 1707530 and nucleotide at position nt1708648. ORF11 encodes a protein similar to a spore coat polysaccharide biosynthesis.

A polynucleotide of interest obtained by the above-disclosed method according to the invention may also contain at least one ORF that encodes all or part of acidic, glycine-rich proteins, belonging to the PE and PPE families, whose genes are often clustered and based on multiple copies of the polymorphic repetitive sequences. The names PE and PPE derive from the fact that the motifs ProGlu (PE, positions 8, 9) and ProProGlu (PPE, positions 7 to 9) are found near the N-terminus in almost all cases. The PE protein family all have a highly conserved N-terminal domain of ~110 amino acid residues, that is predicted to have a globular structure, followed by a C-terminal segment which varies in size, sequence and repeat copy number. Phylogenetic analysis separated the PE family into several groups, the larger of which is the highly repetitive PGRS class containing 55 members whereas the other groups share very limited sequence similarity in their C-terminal domains. The predicted molecular weights of the PE proteins vary considerably as a few members only contain the ~110 amino acid N-terminal domain while the majority have C-terminal extensions ranging in size from 100 up to >1400 residues. A striking feature of the PGRS proteins is their exceptional glycine content (up to 50%) due to the presence of multiple tandem repetitions of GlyGlyAla or GlyGlyAsn motifs or variations thereof.

Like the PE family, the PPE protein family also has a conserved N-terminal domain that comprises ~180 amino acid residues followed by C-terminal segments that vary considerably in sequence and length. These proteins fall into at least three groups, one of which constitutes the MPTR class characterised by the presence of multiple, tandem copies of the motif AsnXGlyXGlyAsnXGly. The second subgroup contains a characteristic, well-conserved motif around position 350 (GlyXXSerValProXXTrp), whereas the other group contains proteins that are unrelated except for the presence of the common 180-residue PPE domain. C-terminal extensions may range in size from 00 up to 3500 residues.

One member of the PGRS sub-family, the WHO antigen 22T (Abou-Zeid et al., 1991), a 55kD protein capable of binding fibronectin, is produced during

disease and elicits a variable antibody response suggesting either that individuals mount different immune responses or that this PGRS-protein may not be produced in this form by all strains of *M. tuberculosis*. In other words, at least some PE_PGRS coding sequences encode for proteins that are involved in the
 5 recognition of *M. tuberculosis* by the immune system of the infected host. Therefore, differences in the PGRS sequences could represent the principal source of antigenic variation in the otherwise genetically and antigenically homogeneous bacterium.

By performing the method of the invention using the *M. tuberculosis* BAC
 10 based DNA library I-1945, the inventors have discovered the occurrence of sequence differences between a given PGRS encoding ORF (ORF reference on the genomic sequence of *M. tuberculosis* Rv0746) of *M. tuberculosis* and its counterpart sequence in the genome of *M. bovis* BCG.

More precisely, the inventors have determined that one ORF contained in
 15 BAC vector N° Rv418 of the *M. tuberculosis* BCG I-1945 DNA library carries both base additions and base deletions when compared with the corresponding ORF in the genome of *M. bovis* BCG that is contained in the BAC vector N° X0175 of the *M. bovis* BCG I-XXXX DNA library. The variations observed in the base sequences correspond to variations in the C-terminal part of the aminoacid
 20 sequence of the PGRS ORF translation product.

As shown in Figure 6, an amino acid stretch of 9 residues in length is present in this *M. tuberculosis* PGRS (ORf reference Rv0746) and is absent from the ORF counterpart of *M. bovis* BCG, namely the following amino acid sequence:

25 NH₂-GGAGGAGGSSAGGGGAGGAGGAGGWLLGD-COOH.

Furthermore, Figure 6 shows also that an amino acid stretch of 45 residues in length is absent from this *M. tuberculosis* PGRS and is present in the ORF counterpart of *M. bovis* BCG, namely following amino acid sequence:

NH₂-GAGGIGGIGGNANGGAGGNGGTGGQLWGSGGAGVEGGAAL
 30 SVGDT-COOH.

Similar observations were made with PPE ORF Rv0442, which showed a 5 codon deletion relative to a *M. bovis* amino acid sequence.

Given that the polymorphism associated with the PE-PGRS or PEE ORFS resulted in extensive antigenic variability or reduced antigen presentation, this
 35 would be of immense significance for vaccine design, for understanding

protective immunity in tuberculosis and, possibly, explain the varied responses seen in different BCG vaccination programmes.

There are several striking parallels between the PGRS proteins and the Epstein-Barr virus-encoded nuclear antigens (EBNA). Both polypeptide families are glycine-rich, contain Gly-Ala repeats that represent more than one third of the molecule, and display variation in the length of the repeat region between different isolates. The Gly-Ala repeat region of EBNA1 has been shown to function as a *cis*-acting inhibitor of antigen processing and MHC class I-restricted antigen presentation (Levitskaya et al., 1995). The fact that MHC class I knock-out mice are extremely susceptible to *M. tuberculosis* underlines the importance of MHC class I antigen presentation in protection against tuberculosis. Therefore, it is possible that the PE/PPE protein family also play some role in inhibiting antigen presentation, allowing the bacillus to hide from the host's immune system.

As such the novel and nonobvious PGRS polynucleotide from *M. bovis* which is homolog to the *M. tuberculosis* ORF Rv0746, and which is contained in the BAC clone N° X0175 (See Table 4 for SP6 and T7 end-sequences of clone n° X0175) of the I-XXXX *M. bovis* BCG BAC DNA library is part of the present invention, as it represents a starting material in order to define specific probes or primers useful for detection of antigenic variability in mycobacterial strains, possible inhibition of antigen processing as well as to differentiate *M. tuberculosis* from *M. bovis* BCG.

Thus, a further object of the invention consists in a polynucleotide comprising the sequence SEQ ID N°4.

Polynucleotides of interest have been defined by the inventors as useful detection tools in order to differentiate *M. tuberculosis* from *M. bovis* BCG. Such polynucleotides are contained in the 45 aminoacid length coding sequence that is present in *M. bovis* BCG but absent from *M. tuberculosis*. This polynucleotide has a sequence beginning (5'end) at the nucleotide at position nt 729 of the sequence SEQ ID N°4 and ending (3'end) at the nucleotide in position nt 863 of the sequence SEQ ID N°4.

Thus, part of the present invention is also a polynucleotide which is chosen among the following group of polynucleotides :

a) a polynucleotide comprising at least 8 consecutive nucleotides of the nucleotide sequence SEQ ID N°5 ;

b) a polynucleotide which sequence is fully complementary to the sequence of the polynucleotide defined in a) ;

c) a polynucleotide that hybridizes under stringent hybridization conditions with the polynucleotide defined in a) or with the polynucleotide defined in b).

5 The stringent hybridization conditions for the purpose of defining the above disclosed polynucleotide are defined herein before in the specification.

 The invention also provides for a BAC-based *Mycobacterium tuberculosis* strain H37Rv genomic DNA library that has been deposited in the Collection Nationale de Cultures de Microorganismes on November 19, 1997 under the
10 accession number I-1945.

 A further object of the invention consists in a recombinant BAC vector which is chosen among the group consisting of the recombinant BAC vectors belonging to the BAC-based DNA library I-1945.

 Generally, a recombinant BAC vector of interest may be chosen among
15 the following set or group of BAC vectors contained in the BAC-based DNA library I-1945 :

Rv101; Rv102; Rv103; Rv104; Rv105; Rv106; Rv107; Rv108; Rv109; Rv10;
Rv110; Rv111; Rv112; Rv113; Rv114; Rv115; Rv116; Rv117; Rv118; Rv119;
Rv11; Rv120; Rv121; Rv122; Rv123; Rv124; Rv126; Rv127; Rv128; Rv129;
20 Rv130; Rv132; Rv134; Rv135; Rv136; Rv137; Rv138; Rv139; Rv13; Rv140;
Rv141; Rv142; Rv143; Rv144; Rv145; Rv146; Rv147; Rv148; Rv149; Rv14;
Rv150; Rv151; Rv152; Rv153; Rv154; Rv155; Rv156; Rv157; Rv159; Rv15;
Rv160; Rv161; Rv162; Rv163; Rv164; Rv165; Rv166; Rv167; Rv169; Rv16;
Rv170; Rv171; Rv172; Rv173; Rv174; Rv175; Rv176; Rv177; Rv178; Rv179;
25 Rv17; Rv180; Rv181; Rv182; Rv183; Rv184; Rv185; Rv186; Rv187; Rv188;
Rv18; Rv190; Rv191; Rv192; Rv193; Rv194; Rv195; Rv196; Rv19; Rv1; Rv201;
Rv204; Rv205; Rv207; Rv209; Rv20; Rv214; Rv215; Rv217; Rv218; Rv219;
Rv21; Rv220; Rv221; Rv222; Rv223; Rv224; Rv225; Rv226; Rv227; Rv228;
Rv229; Rv22; Rv230; Rv231; Rv232; Rv233; Rv234; Rv235; Rv237; Rv240;
30 Rv241; Rv243; Rv244; Rv245; Rv246; Rv247; Rv249; Rv24; Rv251; Rv252;
Rv253; Rv254; Rv255; Rv257; Rv258; Rv259; Rv25; Rv260; Rv261; Rv262;
Rv263; Rv264; Rv265; Rv266; Rv267; Rv268; Rv269; Rv26; Rv270; Rv271;
Rv272; Rv273; Rv274; Rv275; Rv276; Rv277; Rv278; Rv279; Rv27; Rv280;
Rv281; Rv282; Rv283; Rv284; Rv285; Rv286; Rv287; Rv288; Rv289; Rv28;
35 Rv290; Rv291; Rv292; Rv293; Rv294; Rv295; Rv296; Rv29; Rv2; Rv301;

Rv302; Rv303; Rv304; Rv306; Rv307; Rv308; Rv309; Rv30; Rv310; Rv311;
 Rv312; Rv313; Rv314; Rv315; Rv316; Rv317; Rv318; Rv319; Rv31; Rv32;
 Rv322; Rv327; Rv328; Rv329; Rv32; Rv330; Rv331; Rv333; Rv334; Rv335;
 Rv336; Rv337; Rv338; Rv339; Rv33; Rv340; Rv341; Rv343; Rv344; Rv346;
 5 Rv347; Rv348; Rv349; Rv34; Rv350; Rv351; Rv352; Rv353; Rv354; Rv355;
 Rv356; Rv357; Rv358; Rv359; Rv35; Rv360; Rv361; Rv363; Rv364; Rv365;
 Rv366; Rv367; Rv368; Rv369; Rv36; Rv370; Rv371; Rv373; Rv374; Rv375;
 Rv376; Rv377; Rv378; Rv379; Rv37; Rv381; Rv382; Rv383; Rv384; Rv385;
 Rv386; Rv387; Rv388; Rv389; Rv38; Rv390; Rv391; Rv392; Rv393; Rv396;
 10 Rv39; Rv3; Rv40; Rv412; Rv413; Rv414; Rv415; Rv416; Rv417; Rv418; Rv419;
 Rv41; Rv42; Rv43; Rv44; Rv45; Rv46; Rv47; Rv48; Rv49; Rv4; Rv50; Rv51;
 Rv52; Rv53; Rv54; Rv55; Rv56; Rv57; Rv58; Rv59; Rv5; Rv60; Rv61; Rv62;
 Rv63; Rv64; Rv65; Rv66; Rv67; Rv68; Rv69; Rv6; Rv70; Rv71; Rv72; Rv73;
 Rv74; Rv75; Rv76; Rv77; Rv78; Rv79; Rv7; Rv80; Rv81; Rv82; Rv83; Rv84;
 15 Rv85; Rv86; Rv87; Rv88; Rv89; Rv8; Rv90; Rv91; Rv92; Rv94; Rv95; Rv96;
 Rv9.

The end sequences of the polynucleotide inserts of each of the above
 clones corresponding respectively to the sequences adjacent to the T7 promoter
 and to the Sp6 promoter on the BAC vector are shown in Table 3.

20 It has been shown by the inventors that the minimal overlapping set of
 BAC vectors of the BAC-based DNA library I-1945 contains 68 unique BAC
 clones and practically spans almost the whole H37Rv chromosome with the
 exception of a single gap of approximately 150 kb.

25 More specifically, a recombinant BAC vector of interest is chosen among
 the following set or group of BAC vectors from the BAC-based DNA library I-
 1945, the location of which vector DNA inserts on the chromosome of *M.*
tuberculosis is shown in Figure 3 :

Rv234; Rv351; Rv166; Rv35; Rv415; Rv404; Rv209; Rv272; Rv30; Rv228;
 Rv233; Rv38; Rv280; Rv177; Rv48; Rv374; Rv151; Rv238; Rv156; Rv92; Rv3;
 30 Rv403; Rv322; Rv243; Rv330; Rv285; Rv233; Rv219; Rv416; Rv67; Rv222;
 Rv149; Rv279; Rv87; Rv273; Rv266; Rv25; Rv136; Rv414; Rv13; Rv289; Rv60;
 Rv104; Rv5; Rv165; Rv215; Rv329; Rv240; Rv19; Rv74; Rv411; Rv167; Rv56;
 Rv80; Rv164; Rv59; Rv313; Rv265; Rv308; Rv220; Rv258; Rv339; Rv121;
 Rv419; Rv418; Rv45; Rv217; Rv134; Rv17; Rv103; Rv21; Rv22; Rv2; Rv270;
 35 Rv267; Rv174; Rv257; Rv44; Rv71; Rv7; Rv27; Rv191; Rv230; Rv128; Rv407;

Rv106; Rv39; Rv255; Rv74; Rv355; Rv268; Rv58; Rv173; Rv264; Rv417; Rv401; Rv144; Rv302; Rv81; Rv163; Rv281; Rv221; Rv420; Rv175; Rv86; Rv412; Rv73; Rv269; Rv214; Rv287; Rv42; Rv143.

5 The polynucleotides disclosed in Table 3 may be used as probes in order to select a given clone of the BAC DNA library I-1945 for further use.

The invention also provides for a BAC-based *Mycobacterium bovis* strain Pasteur genomic DNA library that has been deposited in the Collection Nationale de Cultures de Microorganismes on XXXX XX, 1998 under the accession number I-XXXX.

10 A further object of the invention consists in a recombinant BAC vector which is chosen among the group consisting of the recombinant BAC vectors belonging to the BAC-based DNA library I-XXXX. This DNA library contains approximately 1600 clones. The average insert size is estimated to be ~80 kb.

15 Generally, a recombinant BAC vector of interest may be chosen among the following set or group of BAC vectors contained in the BAC-based DNA library I-XXXX :

X0001; X0002; X0003; X0004; X0006; X0007; X0008; X0009; X0010; X0012; X0013; X0014; X0015; X0016; X0017; X0018; X0019; X0020; X0021; X0175.

20 The end sequences of the polynucleotide inserts of each of the above clones corresponding respectively to the sequences adjacent to the T7 promoter and to the Sp6 promoter on the BAC vector are shown in Table 4.

The polynucleotides disclosed in Table 4 may be used as probes in order to select a given clone of the BAC DNA library I-XXXX for further use.

25 Are also part of the invention the polynucleotide inserts that are contained in the above described BAC vectors, that are useful as primers or probes.

These polynucleotides and nucleic acid fragments may be used as primers for use in amplification reactions, or as nucleic probes.

30 PCR is described in the US patent N° 4,683,202. The amplified fragments may be identified by an agarose or a polyacrylamide gel electrophoresis, or by a capillary electrophoresis or alternatively by a chromatography technique (gel filtration, hydrophobic chromatography or ion exchange chromatography). The specificity of the amplification may be ensured by a molecular hybridization using, for example, one of the initial primers as nucleic probes.

35 Amplified nucleotide fragments are used as probes in hybridization reactions in order to detect the presence of one polynucleotide according to the

present invention or in order to detect mutations in the genome of the given mycobacterium of interest, specifically a mycobacterium belonging to the *Mycobacterium tuberculosis* complex and more specifically *Mycobacterium tuberculosis* and *Mycobacterium bovis* BCG.

5 Are also part of the present invention the amplified nucleic fragments (« amplicons ») defined herein above.

These probes and amplicons may be radioactively or non-radioactively labeled, using for example enzymes or fluorescent compounds.

10 Other techniques related to nucleic acid amplification may also be used and are generally preferred to the PCR technique.

The Strand Displacement Amplification (SDA) technique (Walker et al., 1992) is an isothermal amplification technique based on the ability of a restriction enzyme to cleave one of the strands at his recognition site (which is under a hemiphosphorothioate form) and on the property of a DNA polymerase to initiate the synthesis of a new strand from the 3'OH end generated by the restriction enzyme and on the property of this DNA polymerase to displace the previously synthesized strand being localized downstream. The SDA method comprises two main steps :

- 15 a) The synthesis, in the presence of dCTP-alpha-S, of DNA molecules that are flanked by the restriction sites that may be cleaved by an appropriate enzyme.
- 20 b) The exponential amplification of these DNA molecules modified as such, by enzyme cleavage, strand displacement and copying of the displaced strands. The steps of cleavage, strand displacement and copy are repeated a sufficient number of times in order to obtain an accurate sensitivity of the assay.

25 The SDA technique was initially realized using the restriction endonuclease HincII but is now generally practised with an endonuclease from *Bacillus stearothermophilus* (BSOBI) and a fragment of a DNA polymerase which is devoid of any 5'→3'exonuclease activity isolated from *Bacillus cladothrix* (exo- Bca) [=exo-minus-Bca]. Both enzymes are able to operate at 30 60°C and the system is now optimized in order to allow the use of dUTP and the decontamination by UDG. When using this technique, as described by Spargo et al. in 1996, the doubling time of the target DNA is of 26 seconds and the amplification rate is of 10^{10} after an incubation time of 15 min at 60°C.

The SDA amplification technique is more easy to perform than PCR (a single thermostated waterbath device is necessary) and is faster than the other amplification methods.

Thus, another object of the present invention consists in using the nucleic acid fragments according to the invention (primers) in a method of DNA or RNA amplification according to the SDA technique. For performing SDA, two pairs of primers are used : a pair of external primers (B1, B2) consisting of a sequence specific for the target polynucleotide of interest and a pair of internal primers (S1, S2) consisting of a fusion oligonucleotide carrying a site that is recognized by a restriction endonuclease, for example the enzyme BSOBI.

The operating conditions to perform SDA with such primers are described in Spargo et al, 1996.

The polynucleotides of the invention and their above described fragments, especially the primers according to the invention, are useful as technical means for performing different target nucleic acid amplification methods such as :

- TAS (Transcription-based Amplification System), described by Kwoh et al. in 1989.
- SR (Self-Sustained Sequence Replication), described by Guatelli et al. in 1990.
- NASBA (Nucleic acid Sequence Based Amplification), described by Kievitis et al. in 1991.
- TMA (Transcription Mediated Amplification).

The polynucleotides according to the invention are also useful as technical means for performing methods for amplification or modification of a nucleic acid used as a probe , such as :

- LCR (Ligase Chain Reaction), described by Landegren et al. in 1988 and improved by Barany et al. in 1991 who employ a thermostable ligase.
- RCR (Repair Chain Reaction) described by Segev et al. in 1992.
- CPR (Cycling Probe Reaction), described by Duck et al. in 1990.
- Q-beta replicase reaction, described by Miele et al. in 1983 and improved by Chu et al. in 1986, Lizardi et al. in 1988 and by Burg et al. and Stone et al. in 1996.

When the target polynucleotide to be detected is a RNA, for example a mRNA, a reverse transcriptase enzyme will be used before the amplification reaction in order to obtain a cDNA from the RNA contained in the biological sample. The generated cDNA is subsequently used as the nucleic acid target for

the primers or the probes used in an amplification process or a detection process according to the present invention.

The non-labeled polynucleotides or oligonucleotides of the invention may be directly used as probes. Nevertheless, the polynucleotides or oligonucleotides are generally labeled with a radioactive element (^{32}P , ^{35}S , ^3H , ^{125}I) or by a non-isotopic molecule (for example, biotin, acetylaminofluorene, digoxigenin, 5-bromodesoxyuridin, fluorescein) in order to generate probes that are useful for numerous applications.

Examples of non-radioactive labeling of nucleic acid fragments are described in the french patent N° FR-7810975 or by Urdea et al. or Sanchez-Pescador et al., 1988.

In the latter case, other labeling techniques may be also used such as those described in the french patents FR-2 422 956 and 2 518 755. The hybridization step may be performed in different ways (Matthews et al., 1988). The more general method consists of immobilizing the nucleic acid that has been extracted from the biological sample onto a substrate (nitrocellulose, nylon, polystyrene) and then to incubate, in defined conditions, the target nucleic acid with the probe. Subsequently to the hybridization step, the excess amount of the specific probe is discarded and the hybrid molecules formed are detected by an appropriate method (radioactivity, fluorescence or enzyme activity measurement).

Advantageously, the probes according to the present invention may have structural characteristics such that they allow the signal amplification, such structural characteristics being, for example, branched DNA probes as those described by Urdea et al. in 1991 or in the European patent N° EP-0 225 807 (Chiron).

In another advantageous embodiment of the probes according to the present invention, the latters may be used as « capture probes », and are for this purpose immobilized on a substrate in order to capture the target nucleic acid contained in a biological sample. The captured target nucleic acid is subsequently detected with a second probe which recognizes a sequence of the target nucleic acid which is different from the sequence recognized by the capture probe.

The oligonucleotide probes according to the present invention may also be used in a detection device comprising a matrix library of probes immobilized on a substrate, the sequence of each probe of a given length being localized in a shift of one or several bases, one from the other, each probe of the matrix library thus

being complementary to a distinct sequence of the target nucleic acid. Optionally, the substrate of the matrix may be a material able to act as an electron donor, the detection of the matrix positions in which an hybridization has occurred being subsequently determined by an electronic device. Such matrix libraries of probes
5 and methods of specific detection of a target nucleic acid is described in the European patent application N° EP-0 713 016 (Affymax technologies) and also in the US patent N° US-5,202,231 (Drmanac).

Since almost the whole length of a mycobacterial chromosome is covered by a BAC-based genomic DNA libraries according to the present invention (i.e. 97% of
10 the *M. tuberculosis* chromosome is covered by the BAC library I-1945), these DNA libraries will play an important role in a plurality of post-genomic applications, such as in mycobacterial gene expression studies where the canonical set of BACs could be used as a matrix for hybridization studies. Probing such matrices with cDNA probes prepared from total mRNA will uncover genetic loci induced or repressed
15 under different physiological conditions (Chuang et al., 1993; Trieselmann et al., 1992). As such, the H37Rv BAC library represents a fundamental resource for present and future genomics investigations.

The BAC vectors or the polynucleotide inserts contained therein may be directly used as probes, for example when immobilized on a substrate such as
20 described herein before.

The BAC vectors or their polynucleotide inserts may be directly adsorbed on a nitrocellulose membrane, at predetermined locations on which one or several polynucleotides to be tested are then put to hybridize therewith.

Preferably, a collection of BAC vectors that spans the whole genome of
25 the mycobacterium under testing will be immobilized, such as, for example, the set of 68 BAC vectors of the I-1945 DNA library that is described elsewhere in the specification and shown in Figure 3.

The immobilization and hybridization steps may be performed as described in the present Materials and Methods Section.

30 As another illustrative embodiment of the use of the BAC vectors of the invention as polynucleotide probes, these vectors may be useful to perform a transcriptional activity analysis of mycobacteria growing in different environmental conditions, for example under conditions in which a stress response is expected, as it is the case at an elevated temperature, for example
35 40°C.

In this specific embodiment of the invention, Genescreen membranes may be used to immobilize the restriction endonuclease digests (*Hind*III digests for the BAC DNA library I-1945) of the BAC vectors by transfer from a gel (Trieselmann et al., 1992).

5 Alternatively, the BAC vectors may be immobilized for dot blot experiments as follows. First, the DNA concentration of each BAC clone is determined by hybridization of blots of clone DNAs and of a BAC vector concentration standard with a BAC vector specific DNA probe. Hybridization is quantified by the Betascope 603 blot analyzer (Betagen Corp.), which collects
10 beta particles directly from the blot with high efficiency. Then, 0.5 µg of each clone DNA is incubated in 0.25 M NaOH and 10 mM EDTA at 65°C for 60 min to denature the DNA and degrade residual RNA contaminants. By using a manifold filtration system (21 by 21 wells), each clone DNA is blotted onto a GeneScreen Plus nylon membrane in the alkaline solution. After neutralization,
15 the blots are baked at 85°C for 2 h under vacuum. Positive and negative controls are added when necessary. In order to perform this procedure, it may be referred to the article of Chuang et al. (1993).

For RNA extractions, cells grown in a suitable volume of culture medium may, for example, be immediately mixed with an equal volume of crushed ice at -
20 70°C and spun at 4°C in a 50 ml centrifugation tube. The cell pellet is then suspended in 0.6 ml of ice-cold buffer (10 mM KCl, 5 mM MgCl, 10 mM Tris; pH 7.4) and then immediately added to 0.6 ml of hot lysis buffer (0.4 M NaCl, 40 mM EDTA, 1% beta-mercaptoethanol, 1% SDS, 20 mM Tris; pH 7.4) containing 100 µl of water saturated phenol. This mixture is incubated in a boiling water
25 bath for 40 s. The debris are removed by centrifugation. The supernatant is extracted with phenol-chloroform five times, ethanol precipitated, and dried. The dried RNA pellet is dissolved in water before use.

Then labeled total cDNA may be prepared by the following method. The reaction mixture contains 15 µg of the previously prepared total RNA, 5 µg of
30 pd(N₆) (random hexamers from Pharmacia Inc.), 0.5 mM dATP, 0.5 mM dGTP and 0.5mM DTTP, 5µM dCTP, 100 µCi of [α -³²P]dCTP (3,000 Ci/mmol), 50 mM Tris-HCl (pH 8.3), 6 mM MgCl₂, 40 mM KCl, 0.5 U of avian myeloblastosis virus reverse transcriptase (Life Science Inc.) in a total volume of 50 µl. The reaction is allowed to continue overnight at room temperature. EDTA and NaOH
35 are then added to final concentrations of 50 mM and 0.25 M, respectively, and

the mixture is incubated at 65°C for 30 min to degrade the RNA templates. The cDNA is then ready to use after neutralization by adding Hcl and Tris buffer.

The hybridization step may be performed as described by Chuang et al. (1993) and briefly disclosed hereinafter. The DNA dot blot is hybridized to ³²P-labeled total cDNA in a solution containing 0.1% polyvinylpyrrolidone, 0.1% Ficoll, 0.1% sodium Pp_i, 0.1% bovine serum albumin, 0.5% SDS, 100 mM NaCl, and 0.1 mM sodium citrate, pH 7.2, at 65°C for 2 days and then washed with a solution containing 0.1% SDS, 100 mM NaCl, and 10 mM Na-citrate, pH 7.2. The same dot blot is used for hybridization with both control and experimental cDNAs, with an alkaline probe stripping procedure (soaked twice in 0.25M NaOH-0.75 M NaCl at room temperature, 30 min each, neutralized, and completely dried at 65°C for at least 30 min) between the two hybridizations. Quantification may be done with the Betascope 603 blot analyzer (Betagen Corp.).

As it flows from the above technical teachings, another object of the invention consists in a method for detecting the presence of mycobacteria in a biological sample comprising the steps of :

- a) bringing into contact the recombinant BAC vector or a purified polynucleotide according to the invention with a biological sample ;
- b) detecting the hybrid nucleic acid molecule formed between said purified polynucleotide and the nucleic acid molecules contained within the biological sample.

The invention further deals with a method for detecting the presence of mycobacteria in a biological sample comprising the steps of :

- a) bringing into contact the recombinant BAC vector or a purified polynucleotide according to the invention that has been immobilized onto a substrate with a biological sample ;
- b) bringing into contact the hybrid nucleic acid molecule formed between said purified polynucleotide and the nucleic acid contained in the biological sample with a labeled recombinant BAC vector or a polynucleotide according to the invention, provided that said polynucleotide and polynucleotide of step a) have non-overlapping sequences.

Another object of the invention consists in a method for detecting the presence of mycobacteria in a biological sample comprising the steps of :

- a) bringing into contact the nucleic acid molecules contained in the biological sample with a pair of primers according to the invention;
- b) amplifying said nucleic acid molecules;
- c) detecting the nucleic acid fragments that have been amplified, for example by gel electrophoresis or with a labeled polynucleotide according to the invention.

In one specific embodiment of the above detection and/or amplification methods, said methods comprise an additional step wherein before step a), the nucleic acid molecules of the biological sample have been made available to a hybridization reaction.

- 10 In another specific embodiment of the above detection methods, said methods comprise an additional step, wherein, before the detection step, the nucleic acid molecules that are not hybridized with the immobilized purified polynucleotide are removed.

Also part of the invention is a kit for detecting mycobacteria in a biological sample comprising :

- a) a recombinant BAC vector or a purified polynucleotide according to the invention;
- b) reagents necessary to perform a nucleic acid hybridization reaction.

20 The invention also pertains to a kit for detecting a mycobacteria in a biological sample comprising :

- a) a recombinant BAC vector or a purified polynucleotide according to the invention that is immobilized onto a substrate;
- b) reagents necessary to perform a nucleic acid hybridization reaction;
- c) a purified polynucleotide according to the invention which is radioactively or non-radioactively labeled, provided that said polynucleotide and the polynucleotide of step a) have non-overlapping sequences.

Moreover, the invention provides for a kit for detecting mycobacteria in a biological sample comprising :

- a) a pair of purified primers according to the invention;
- b) reagents necessary to perform a nucleic acid amplification reaction;
- c) optionally, a purified polynucleotide according to the invention useful as a probe.

35 The invention embraces also a method for detecting the presence of a genomic DNA, a cDNA or a mRNA of mycobacteria in a biological sample, comprising the steps of :

a) bringing into contact the biological sample with a plurality of BAC vectors according to the invention or purified polynucleotides according to the invention, that are immobilized on a substrate;

b) detecting the hybrid complexes formed.

5 The invention also provides a kit for detecting the presence of genomic DNA, cDNA or mRNA of a mycobacterium in a biological sample, comprising :

a) a substrate on which a plurality of BAC vectors according to the invention or purified polynucleotides according to the invention have been immobilized;

b) optionally, the reagents necessary to perform the hybridization reaction.

10 Additionally, the recombinant BAC vectors according to the invention and the polynucleotide inserts contained therein may be used for performing detection methods based on « molecular combing ». Said methods consist in methods for aligning macromolecules, especially DNA and are applied to processes for detecting, for measuring intramolecular distance, for separating and/or for
15 assaying a macromolecule, especially DNA in a sample.

These « molecular combing » methods are simple methods, where the triple line S/A/B (meniscus) resulting from the contact between a solvent A and the surface S and a medium B is caused to move on the said surface S, the said macromolecules (i.e. DNA) having a part, especially an end, anchored on the
20 surface S, the other part, especially the other end, being in solution in the solvent A. These methods are particularly fully described in the PCT Application n° PCT/FR 95/00165 filed on February 11, 1994 (Bensimon et al.).

When performing the « molecular combing » method with the recombinant BAC vectors according to the inventions or their polynucleotide inserts, the
25 latters may be immobilized (« anchored ») on a suitable substrate and aligned as described in the PCT Application n° PCT/FR 95/00165, the whole teachings of this PCT Application being hereby incorporated by reference. Then, polynucleotides to be tested, preferably under the form of radioactively or non radioactively labeled polynucleotides, that may consist of fragments of genomic
30 DNA, cDNA etc. are brought into contact with the previously aligned polynucleotides according to the present invention and then their hybridization position on the aligned DNA molecules is determined using any suitable means including a microscope or a suitable camera device.

Thus, the present invention is also directed to a method for the detection
35 of the presence of a polynucleotide of mycobacterial origin in a biological sample

and/or for physical mapping of a polynucleotide on a genomic DNA, said method comprising :

- a) aligning at least one polynucleotide contained in a recombinant BAC vector according to the invention on the surface of a substrate;
- 5 b) bringing into contact at least one polynucleotide to be tested with the substrate on which the at least one polynucleotide of step a) has been aligned;
- c) detecting the presence and/or the location of the tested polynucleotide on the at least one aligned polynucleotide of step a).

The invention finally provides for a kit for performing the above method,
10 comprising :

- a) a substrate whose surface has at least one polynucleotide contained in a recombinant BAC vector according to the invention;
- b) optionally, reagents necessary for labeling DNA;
- c) optionnally, reagents necessary for performing a hybridization reaction.

15 In conclusion, it may be underlined that the alliance of such BAC-based approaches such as described in the present specification to the advances in comparative genomics by the availability of an increased number of complete genomes, and the rapid increase of well-characterized gene products in the public databases, will allow the one skilled in the art an exhaustive analysis of the
20 mycobacterial genome.

MATERIALS AND METHODS

1. **DNA-preparation.** Preparation of *M. tuberculosis* H37Rv DNA in agarose plugs was conducted as previously described (Canard et al., 1989; Philipp et al.,
25 1996b). Plugs were stored in 0.2 M EDTA at 4°C and washed 3 times in 0.1% Triton X-100 buffer prior to use.

2. **BAC vector preparation.** pBeloBAC11 was kindly provided by Dr. Shizuya, Department of Biology, California Institute of Technology (Pasadena, CA). The preparation followed the description of Woo et al., 1994 (Woo et al., 1994).

30 3. **Partial digestion with *Hind*III.** Partial digestion was carried out on plugs, each containing approximately 10 µg of high molecular weight DNA, after three one hour equilibration steps in 50 ml of *Hind*III 1X digestion buffer (Boehringer Mannheim, Mannheim, Germany) plus 0.1% Triton X-100. The buffer was then removed and replaced by 1ml/plug of ice-cold *Hind*III enzyme buffer containing
35 20 units of *Hind*III (Boehringer). After two hours incubation on ice, the plugs

were transferred to a 37°C water bath for 30 minutes. Digestions were stopped by adding 500 µl of 50 mM EDTA (pH 8.0).

4. **Size selection.** The partially digested DNA was subjected to contour-clamped homogenous electric field (CHEF) electrophoresis on a 1% agarose gel using a
5 BioRad DR III apparatus (BioRad, Hercules, CA) in 1X TAE buffer at 13°C, with a ramp from 3 to 15 seconds at 6 V/cm for 16 hours. Agarose slices from 25 to 75 kb, 75 to 120 kb and 120 to 180 kb were excised from the gel and stored in TE at 4°C.

5. **Ligation and transformation.** Agarose-slices containing fractions from 25 to
10 75 kb, 75 to 120 kb and 120 to 180 kb were melted at 65°C for 10 minutes and digested with Gelase (Epicentre Technologies, Madison, WI), using 1 unit per 100 µl gel-slice. 25-100 ng of the size-selected DNA was then ligated to 10 ng of *Hind*III digested, dephosphorylated pBeloBAC11 in a 1:10 molar ratio using 10 units of T4 DNA ligase (New England Biolabs, Beverly, MA) at 16°C for 20
15 hours. Ligation mixtures were heated at 65°C for 15 minutes, then drop-dialysed against TE using Millipore VS 0.025 mM membranes (Millipore, Bedford, MA). Fresh electrocompetent *E. coli* DH10B cells (Sheng et al., 1995) were harvested from 200 ml of a mid-log (OD₅₅₀=0.5) culture grown in SOB medium. Cells were washed three times in ice-cold water, and finally resuspended in ice-cold
20 water to a cell density of 10¹¹ cells/ml (OD₅₅₀=150). 1 µl of the ligation-mix was used for electroporation of 30 µl of electrocompetent DH10B *E. coli* using a Eurogentec Easyject Plus electroporator (Eurogentec, Seraing, Belgium), with settings of 2.5 kV, 25 µF, and 99 Ω, in 2 mm wide electroporation cuvettes. After electroporation, cells were resuspended in 600 µl of SOC medium, allowed to
25 recover for 45 minutes at 37°C with gentle shaking, and then plated on LB agar containing 12.5 µg/ml chloramphenicol (CM), 50 µg/ml X-gal, and 25 µg/ml IPTG. The plates were incubated overnight and recombinants (white colonies) were picked manually to 96 well plates. Each clone was inoculated 3 times (2 X 200 µl and 1 X 100 µl of 2YT/12.5 µg/ml CM per clone) and incubated
30 overnight. One of the microtiter plates, containing 100 µl culture per well, was maintained as a master plate at -80°C after 100 ml of 80% glycerol were added to each well, while minipreps (Sambrook et al., 1989) were prepared from the remaining two plates to check for the presence of inserts. Clones containing inserts were then designated "Rv" clones, repicked from the master plate to a
35 second set of plates for storage of the library at -80°C.

6. **Preparation of DNA for sizing, direct sequencing and comparative genomics.** A modified Birnboim and Doly protocol (Birnboim et al., 1979) was used for extraction of plasmid DNA for sequencing purposes. Each Rv clone was inoculated into a 50 ml Falcon polypropylene tube containing 40 ml of 2YT medium with 12.5 µg/ml of CM and grown overnight at 37°C with shaking. Cells were harvested by centrifugation and stored at -20°C. The frozen pellet was resuspended in 4 ml of Solution A (50 mM glucose, 10 mM EDTA, 25 mM Tris, pH 8.0) and 4 ml of freshly prepared solution B (0.2 M NaOH, 0.2% SDS) was then added. The solution was gently mixed and kept at room temperature for 5 minutes before adding 4 ml of ice-cold solution C (3M Sodium Acetate, pH 4.7). Tubes were kept on ice for 15 min, and centrifuged at 10,000 rpm for 15 min. After isopropanol precipitation, the DNA pellet was dissolved in 600 µl RNase solution (15 mM Tris HCl pH 8.0, 10 µg/ml RNase A). After 30 minutes at 37°C the DNA solution was extracted with chloroform:isoamylalcohol (24:1) and precipitated from the aqueous phase using isopropanol. The DNA pellet was then rinsed with 70% ethanol, air-dried and dissolved in 30 µl distilled water. In general, DNA prepared by this method was clean and concentrated enough to give good quality results by automatic sequencing (at least 300 bp of sequence). For a few DNA preparations, an additional polyethylene glycol (PEG) precipitation step was necessary, which was performed as follows. The 30 µl of DNA solution were diluted to 64µl, mixed gently and precipitated using 16 µl 4M NaCl and 80 µl of 13% PEG 8000. After 30 min on ice the tubes were centrifuged at 4°C, the pellet carefully rinsed with 70% ethanol, air-dried and diluted in 20 µl of distilled water.
7. **Sizing of inserts.** Insert sizes were determined by pulsed-field gel electrophoresis (PFGE) after cleavage with *DraI* (Promega). 100-200 ng of DNA was *DraI*-cleaved in 20 µl total reaction volume, following the manufacturer's recommendations, then loaded onto a 1% agarose gel and migrated using a pulse of 4 s for 15 h at 6.25 V/cm at 10°C on an LKB-Pharmacia CHEF apparatus. Mid-range and low-range PFGE markers (New England Biolabs) were used as size standards. Insert sizes were estimated after ethidium bromide staining of gels.
8. **Direct sequencing.** For each sequencing reaction 7 µl BAC DNA (300-500ng), 2 µl primer (2 µM), 8 µl reaction mix of the *Taq* DyeDeoxy Terminator cycle sequencing kit (Applied Biosystems) and 3 µl distilled water were used.

After 26 cycles (96°C for 30 sec; 56°C for 15 sec; 60°C for 4 min) in a thermocycler (MJ-research Inc., Watertown, MA) DNA was precipitated using 70 µl of 70% ethanol/0.5 mM MgCl₂, centrifuged, rinsed with 70% ethanol, dried and dissolved in 2 µl of formamide/EDTA buffer. SP6 and T7 samples of 32 BAC clones were loaded onto 64 lane, 6% polyacrylamide gels and electrophoresis was performed on a Model 373A automatic DNA sequencer (Applied Biosystems) for 12 to 16 hours. The sequences of oligonucleotides used as primers are shown in Table 1.

9. DOP-PCR. As an alternate procedure we used partially degenerate oligonucleotides in combination with vector-specific (SP6 or T7) primers to amplify insert ends of BAC clones, following a previously published protocol for P1 clones (Liu et al., 1995). The degenerate primers Deg2, Deg3, Deg4, Deg6 (Table 1) gave the best results for selected amplification of insert termini.

Table 1: Primers used for PCRs and sequencing

Vector specific Primers for DOP PCR- first amplification step:

SP6-BAC1: AGT TAG CTC ACT CAT TAG GCA

T7-BAC1 : GGA TGT GCT GCA AGG CGA TTA

Vector specific Primers (direct sequencing, nested primer for second PCR step)

SP6 Mid: AAA CAG CTA TGA CCA TGA TTA CGC CAA

T7-Belo2: TCC TCT AGA GTC GAC CTG CAG GCA

Degenerate Primers:

Deg2: TCT AGA NNN NNN TCC GGC

Deg3: TCT AGA NNN NNN GGG CCC

Deg4: CGT TTA AAN NNN NWA GGC CG

Deg6: GGT ACT AGT NNN NNW TCC GGC

Primers used for the amplification of *M. bovis* DNA in polymorphic chromosomal region of Rv58:

Primer 1: ACG ACC TCA TAT TCC GAA TCC C

Primer 2: GCA TCT GTT GAG TAC GCA CTT CC

10. Screening by pooled PCR. To identify particular clones in the library which could not be detected by random end-sequencing of the 400 BAC clones, PCR-screening of DNA pools was performed. Primers were designed for regions of the chromosome where no BAC coverage was apparent using cosmid-or H37Rv

whole genome shotgun sequences. Primers were designed to amplify approximately 400-500 bp. Ninety-six-well plates containing 200 μ l 2YT/12.5 μ g/ml CM per well were inoculated with 5 μ l of -80°C glycerol stock cultures each from the master plates and incubated overnight. The 96 clones of each plate were pooled by taking 20 μ l of culture from each well and this procedure was repeated for 31 plates. Pooled cultures were centrifuged, the pellets were resuspended in sterile water, boiled for 5 minutes, centrifuged and the supernatants kept for PCRs. As an initial screening step, the 31 pools of a total of 2976 BACs, representing about two thirds of the library were tested for the presence of a specific clone using appropriate PCR primers. PCR was performed using 10 μ l of supernatant, 5 μ l of assay buffer (100 mM β -mercaptoethanol, 600 mM Tris HCl (pH 8.8), 20 mM $MgCl_2$, 170 mM $(NH_4)_2SO_4$), 5 μ l of Dimethylsulfoxide (DMSO), 5 μ l of dNTPs (20 mM), 5 μ l of water, 10 μ l primer (2 μ M), 10 μ l inverse primer (2 μ M) and 0.2 units of *Taq* DNA polymerase (Boehringer). 32 cycles of PCR (95°C for 30 s, 55°C for 1 min 30 s, 72°C for 2 min) were performed after an initial denaturation at 95°C for 1 min. An extension step at 72 °C for 5 min finished the PCR. If a pool of 96 clones yielded an appropriate PCR product (Fig. 1A), subpools were made to identify the specific clone. Subpools representative for lane A of a 96 well plate were made by pooling clones 1 to 12 from lane A into a separate tube. Subpools for lanes B to H were made in the same way. In addition, subpools of each of the 12 rows (containing 8 clones each) were made, so that for one 96 well plate, 20 subpools were obtained. PCR with these 20 subpools identified the specific clone (Fig. 1B, lower gel portion). If more than one specific clone was present among the 96 clones of one plate (Fig. 1B, upper gel portion), additional PCR reactions had to be performed with the possible candidates (data not shown).

11. Genomic comparisons. DNA from the BAC clone Rv58 was digested with the restriction endonucleases *Eco*RI and *Pvu*II, and resolved by agarose gel electrophoresis at low voltage overnight (1.5 V/cm). DNA was transferred via the method of Southern to nitrocellulose membranes (Hybond C extra, Amersham) following standard protocols (Sambrook et al., 1989), then fixed to the membranes at 80°C for 2 hours. The blot was hybridized with ³²P labelled total genomic DNA from *M. tuberculosis* H37Rv, *M. bovis* type strain (ATCC 19210) or *M. bovis* BCG Pasteur. Hybridization was performed at 37°C overnight in

50% formamide hybridization buffer as previously described (Philipp et al., 1996b). Results were interpreted from the autoradiograms.

12. **Computer analysis.** Sequence data from the automated sequencer ABI373A were transferred as binary data to a Digital Alpha 200 station or Sun SparcII station and analysed using TED, a sequence analysis program from the Staden software package (Dear et al., 1991). Proof-read sequences were compared using the BLAST programs (Altschul et al., 1990) to the *M. tuberculosis* H37Rv sequence databases of the Sanger Centre, containing the collected cosmid sequences (TB.dbs) and whole-genome shotgun reads (TB_shotgun_all.dbs) (http://www.sanger.ac.uk/). In addition, local databases containing 1520 cosmid end-sequences and the accumulating BAC end-sequences were used to determine the exact location of end-sequenced BACs on the physical and genetic map. MycDB (Bergh et al., 1994) and public databases (EMBL, Genbank) were also used to compare new sequences, but to a lesser extent. The organization of the open reading frames (ORFs) in the polymorphic region of clone Rv58 was determined using the DIANA software established at the Sanger Centre.

EXAMPLES

Example 1 : Construction of a pBeloBAC11 library of *M. tuberculosis* H37Rv.

Partial *Hind*III fragments of H37Rv DNA in the size range of 25 to 180 kb were ligated into pBeloBAC11 and electroporated into strain *E. coli* DH10B. While cloning of fractions I (25 to 75 kb) and II (75 to 120 kb) gave approximately 4×10^4 transformants (white colonies), cloning of fraction III (120 to 180 kb) repeatedly resulted in empty clones. Parallel cloning experiments using partial *Hind*III digests of human DNA resulted in stable inserts for all three fractions (data not shown), suggesting that the maximum size of large inserts in BAC clones is strongly dependent on the source of the DNA. Analysis of the clones for the presence of inserts revealed that 70 % of the clones had an insert of the appropriate size while the remaining 30% of white colonies represented empty or *lacZ'*-mutated clones. Size determination of randomly selected, *Dra*I-cleaved BACs via PFGE showed that the insert sizes ranged for the majority of the clones between 40 kb and 100 kb with an average size of 70 kb. Clones with inserts of appropriate size were designated with "Rv" numbers, recultured and stored at -80°C for further use.

Example 2 : Direct DNA sequence analysis of BACs.

To characterize the BAC clones, they were systematically subjected to insert termini sequencing. Two approaches, direct sequencing of BAC DNA and PCR with degenerate oligonucleotide primers (DOP), adapted to the high G+C content of mycobacterial DNA, were used. In a first screening phase, 50 BAC clones designated Rv1 to Rv50 were analysed using both methods in parallel. Except for two clones, where the sequences diverged significantly, the sequences obtained by the two methods only differed in length. Sequences obtained directly were on average about 350 bp long and for 95% of the clones both the SP6 and T7 end-sequences were obtained at the first attempt. Sequences obtained by DOP-PCR were mostly shorter than 300 bp. For 40% of the BACs we obtained only very short amplicons of 50 to 100 base pairs from one end. In two cases the sequence obtained with the DOP-PCR differed from the sequences obtained by direct sequencing, and in these cases *E.coli* or vector sequences were amplified (data not shown). Taking the advantages and disadvantages of both methods into account, we decided to use direct termini sequencing for the systematic determination of the SP6 and T7 end-sequences.

Example 3 : Representativity of the library.

After having determined the end-sequences of 400 BACs a certain redundancy was seen. The majority of clones were represented at least 3 to 4 times. Maximum redundancy was seen in the vicinity of the unique *rrn* operon, as 2.5 % of the clones carried identical fragments that bridge the cosmids Y50 and Y130 (Fig. 3, approximate position at 1440 kb). The majority of clones with identical inserts appeared as two variants, corresponding to both possible orientations of the *HindIII* fragment in pBeloBAC11. This suggests that the redundancy was not the result of amplification during library construction, but due to the limited number of possible combinations of partial *HindIII* fragments in the given size-range of 25 to 120 kb. To detect rare BAC clones, a pooled PCR protocol was used. Primers were designed on the basis of the existing cosmid sequences and used to screen 31 pools of 96 BAC clones. When positive PCR products of the correct size were obtained, smaller subpools (of 8 or 12 clones each) of the corresponding pool were subsequently used to identify the corresponding clone (Figs. 1A and 1B). With this approach 20 additional BACs (Rv401-Rv420) were found for the regions where no BACs were found with the initial systematic sequencing approach. The end-sequences of these BACs

(Rv401-420) were determined by direct sequencing, which confirmed the predicted location of the clones on the chromosome. A 97% coverage of the genome of H37Rv with BAC clones was obtained. Only one region of ~ 150 kb was apparently not represented in the BAC library as screening of all pools with several sets of specific primers did not reveal the corresponding clone. This was probably due to the fact that *Hind*III fragments of mycobacterial DNA larger than 110 kb are very difficult to establish in *E. coli* and that a *Hind*III fragment of ~120 kb is present in this region of the chromosome (data not shown).

Example 4 : Establishing a BAC map.

Using all end-sequence and shotgun-sequence data from the H37Rv genome sequencing project, most of the BAC clones could then be localized by sequence comparison on the integrated map of the chromosome of *M. tuberculosis* strain H37Rv (Philipp et al., 1996b) and an ordered physical map of the BAC-clones was established. PCR with primers from the termini sequences of selected BACs were used for chromosomal walking and confirmation of overlapping BACs (data not shown). The correct order of BACs on the map was also confirmed more recently, using 40,000 whole genome shotgun reads established at the Sanger Centre. In addition, pulsed-field gel electrophoresis of *Dra*I digests of selected BACs was performed (Fig. 2) in order to see if the approximate fragment size and the presence or absence of *Dra*I cleavage sites in the insert were consistent with the location of the BACs on the physical map (Fig. 3). Comparison of the sequence-based BAC-map with the physical and genetic map, established by PFGE and hybridization experiments (Philipp et al., 1996b), showed that the two maps were in good agreement. The positions of 8 genetic markers previously shown on the physical and genetic map were directly confirmed by BAC-end-sequence data (Table 2, Fig. 3). The position of 43 from 47 Y-clones (91%) shown on the physical and genetic map, which were later shotgun sequenced, was confirmed by the BAC end-sequences and shotgun sequence data. Four clones (Y63, Y180, Y251, and Y253) were located to different positions than previously thought and this was found to be due to book keeping errors or to chimeric inserts. Their present approximate location relative to the *oriC* is shown in Figure 3: Y63 at 380 kb, Y63A at 2300 kb, Y180 at 2160 kb, Y251 at 100 kb, and Y253 at 2700 kb. A total of 48 BACs, covering regions of the chromosome, not represented by cosmids were then shotgun sequenced (Cole et al., 1997), and these are squared in Fig. 3. No chimeric BACs

were found, which is consistent with the observations of other research groups for other BAC libraries (Cai et al., 1995; Zimmer et al., 1997). The absence of chimeric BACs was of particular importance for the correct assembly of the *M. tuberculosis* H37Rv sequence. The exact position of the BAC termini sequences on the chromosome will be available via the world wide web (<http://www.pasteur.fr/MycDB>).

Table 2 : Identities of genetic markers previously shown on the integrated and genetic map of H37Rv (Phlipp et al., 1996b) wich showed perfect sequence homology with BAC ens sequences.

Locus	BAC end sequence	Description of genetic marker	Organism	GenBank Accession n°
<i>apa</i>	Rv163SP6	Secreted alanine-proline-rich antigen	<i>M. tuberculosis</i>	X80268
<i>dnaJ, dnaK</i>	Rv164T7	DnaJ hsp	<i>M. leprae</i>	M95576
<i>fop-A</i>	Rv136T7	Fibronectin binding protein	<i>M. tuberculosis</i>	M27016
<i>polA</i>	Rv401T7	DNA polymerase I	<i>M. tuberculosis</i>	L11920
<i>ponA</i>	Rv273T7	Penicillin binding protein	<i>M. leprae</i>	S82044
<i>pslC</i>	Rv103T7	Putative phosphate transport receptor	<i>M. tuberculosis</i>	Z48057
<i>recA</i>	Rv415SP6	Homologous recombination	<i>M. tuberculosis</i>	X58485
<i>wag9</i>	Rv35SP6	35-kDa antigen	<i>M. tuberculosis</i>	M69187

Example 5 : Repetitive end-sequences.

Repetitive sequences can seriously confound mapping and sequence assembly. In the case of the BAC end-sequences, no particular problems with repetitive sequences were observed. Although nine clones with one end in an *IS1081* (Collins et al., 1991) sequence were identified, it was possible to correctly locate their position on the map using the sequence of the second terminus. Moreover, these BACs were used to determine the exact locations of *IS1081* sequences on the map. Five copies of this insertion sequence, which

harbors a *Hind*III cleavage site, were mapped on the previous physical and genetic map. In contrast, BAC end-sequence data revealed an additional copy of *IS1081* on the *M. tuberculosis* H37Rv chromosome. The additional copy was identified by six clones (Rv27, Rv118, Rv142, Rv160, Rv190, Rv371) which harbored an identical fragment linking Y50 to I364 (Fig. 3, at ~ 1380 kb). This copy of *IS1081* was not found by previous hybridization experiments probably because it is located near another copy of *IS1081*, localized on the same *Dra*I fragment Z7 and *Asn*I fragment U (Fig. 3, at ~ 1140 kb). Furthermore, the position of a copy of *IS1081* previously shown in *Dra*I fragment Y1 (Fig. 3, at ~ 1840 kb) had to be changed to the region of Y349 (Fig. 3, at ~ 3340 kb) according to the end-sequences of BAC Rv223. The positions of the four other *IS1081* copies were confirmed by the sequence data and therefore remained unchanged. In total 6 copies of *IS1081* were identified in the H37Rv genome in agreement with the findings of others (Collins et al., 1991).

In addition, a sequence of 1165 bp in length containing a *Hind*III site was found in two copies in the genome of H37Rv in different regions. The end-sequences of BAC clones Rv48 and Rv374, covering cosmid Y164, as well as Rv419 and Rv45, that cover cosmid Y92, had perfect identity with the corresponding parts of this 1165 bp sequence (Fig. 3, at ~ 3480 kb and ~ 900 kb). Analysis of the sequence did not reveal any homology with insertion sequences or other repetitive elements. However, as each of the two locations showed appropriate BAC coverage, chimerism of the sequenced cosmids Y164 and Y92 can be ruled out as the probable cause.

Example 6 : Using BAC clones in comparative genomics.

The minimal overlapping set of BAC clones represents a powerful tool for comparative genomics. For example, with each BAC clone containing on average an insert of 70 kb, it should be possible to cover a 1Mb section of the chromosome with 15 BAC clones. Restriction digests of overlapping clones can then be blotted to membranes, and probed with radiolabelled total genomic DNA from, for example, *M. bovis* BCG Pasteur. Restriction fragments that fail to hybridize with the *M. bovis* BCG Pasteur DNA must be absent from its genome, hence identifying polymorphic regions between *M. bovis* BCG Pasteur and *M. tuberculosis* H37Rv. The results of such an analysis with clone Rv58 (Fig. 3, at ~1680 kb) are shown here. This clone covers a previously described polymorphic genomic region between *M. tuberculosis* and *M. bovis* BCG strains (Philipp et

al., 1996a). *EcoRI* and *PvuII* digests from clone Rv58, fixed on nitrocellulose membranes, were hybridized with ³²P-labelled total genomic DNA from *M. tuberculosis* H37Rv, *M. bovis* (ATCC 19120), and *M. bovis* BCG Pasteur. Figures 4A and 4B present the results of this analysis, where it is clear that several restriction fragments from clone Rv58 failed to hybridize with genomic DNA from either *M. bovis* or *M. bovis* BCG Pasteur. On the basis of the various missing restriction fragments, a restriction map of the polymorphic region was established and compared to the H37Rv sequence data. The localization of the polymorphism could therefore be estimated, and appropriate oligonucleotide primers (Table 1) were selected for the amplification and sequencing of the corresponding region in *M. bovis*. The alignment of *M. bovis* and *M. tuberculosis* H37Rv sequences showed that 12,732 bp were absent from the chromosomal region of the *M. bovis* type strain and *M. bovis* BCG Pasteur strain. The G+C content of the polymorphic region is 62.3 mol%, which is the same as the average genome G+C content of the *M. tuberculosis* genome, hence indicating that this region is not a prophage or other such insertion. Subsequent PCR studies revealed that this segment was also absent from the Danish, Russian, and Glaxo substrains of *M. bovis* BCG, suggesting that this polymorphism can be used to distinguish *M. bovis* from *M. tuberculosis*. Analysis of this sequence showed that 11 putative open reading frames (ORFs) are present in *M. tuberculosis*, corresponding to ORFs MTCY277.28 to MTCY277.38 / accession number Z79701 -EMBL Nucleotide Sequence Data Library (Fig. 5). FASTA searches against the protein and nucleic acid databases revealed that the genes of this region may be involved in polysaccharide biosynthesis. Among these putative genes, the highest score was seen with ORF 6 (MTCY277.33), whose putative product shows a 51.9% identity with GDP-D-Mannose dehydratase from *Pseudomonas aeruginosa* (accession number U18320 - EMBL Nucleotide Sequence Data Library) in a 320 amino acid overlap. The novel *M. bovis* sequence of the polymorphic region was deposited under accession number AJ003103 in the EMBL Nucleotide Sequence Data Library.

As it appears from the teachings of the specification, the invention is not limited in scope to one or several of the above detailed embodiments; the present invention also embraces all the alternatives that can be performed by one skilled in the same technical field, without deviating from the subject or from the scope of the instant invention.

Table 3 : End-sequences of the polynucleotide inserts cloned in the named recombinant BAC vectors contained in the I-1945 *M. tuberculosis* H37Rv genomic DNA library.

RvXXXSP6 corresponds to the SP6 end-sequence of the clone RvXXX.

RvXXXT7 corresponds to the T7 end-sequence of the clone RvXXX.

RvXXXIS 1081 corresponds to a region located close to a copy of the IS1081 repetitive sequence (Insertion element).

The character « - » denotes an uncertain base residue.

Clone Rv101

.....Rv101SP6.seq:.....

AATACTCAAGCTTGCCAGCCGTCGATGACAAGAAATATGTCCGCAAAAGACTCAGCGGGCCGACTTTGCTCGCAGCTG
GCGGTACCGCGCCACCGATTCTATGCCGTGGTTCGCGGAAAAATGCCCTCCCGAAATCGCACGGCCGACTCCAGTTCCGGC
GAGCATCCGCGATGCCAGCTGCGGCTGCGCCCTGCCGGCCACGGCACCACATGCGGCAGTTTCGTCCACCTGGGCCAG
CGCCCCGCGCCGAATTCCAAACAATAGAACTGCACCCGCGCCGCATCGTGGGTAAACAGCCAACGCCATGATCAGCGT
CCGCAGCGCGTTGACTTGCCCGTTTGGCGGTGCACCTACGAACGCGACATTGCCCTGCGGCCCCGGACAAGTCGATCGT
GCGCGGCACCCGTGACTGCTCTAACGGGCGATTGAAATTCCGAT

.....Rv101T7.seq:.....

CCACCCGTGTAATTTGGGATGGGCAAAAAGGCGAAGCACC CGTGGCCACGAACGCCGGGAGGGACAATCTCGGGCGG
TTAGGGCTTCTCGCGGGAAGGCCCGAACGTACGGCGTTTCAACACCTCGCGTCGCCCTCCGACCGCGAACATTTCGGGG
ATGGCAGCAACCTGCTGGCACCCTGGCCGGGCGATGATCTGCAGCGTCGCCCGGGGTAGTCGCCCGCCGGGCGGCTAC
ACTCTGAAACGCGATGACCATCGATGTGTGGATGCAGCATCCCGACGCAACGGTTCCTACACCGCGATATGTTTCGCT
CGCTGCCCCGGTGGACCGT

Clone Rv102

.....Rv102SP6.seq:.....

AATACTCAAGCTTTCCGCCGATACCCGCCATGTCGCGCACATCCAGGACTTCTGGGGGGATCCGCTGACAGCGGGCGG
ATCCCAAAGTGCGGATGATCGGGCCGCTACGTCTGTGGTGTACCTCGTCGGTAACAACGAAACCGAAGCGTATGACTC
GGTCCACGCGGTGCGGCACATGGTGGACACCACCCGCCACCGCAACGGGTGAAGGCCTATGTACCCGGTCCGGCAGC
ACTCAATGCCGACCAGGCCGAGGGCGGAGACAAAAGTATCGCTAAGGTCACCGCGATCACCACATGGTGATCGCAGC
AATGTTGCTAGTGATCTATCGCTCCGTAATTACCGCGTTCT

.....Rv102T7.seq:.....

GTGCCGTTCCAACCCGAATTGGCTTTCCGGCGCCATCGGTGAGGACGGCGTGC GG GTGCTCAACGACGACGTCTGCCG
GGGACACACCTCGATGCTGCCGCCATGGACGCGGTGCAACGCAAGCAGCTGATCGAGCTACAACGCCGCGCGGAACGC
TTCCGCCGCGGGCGTGACCGCATCCCGTTGACCGGGCGGATCGCGGTGATCGTCGATGACGGCATCGCCACCGGAGCG
ACGGCCAAGGCGGCGTGCCAGGTGCGCCGGGCGCACGGTGCGGACAAGGTGGTGGTGGCGGTCCCGATCGGCCAGAC
GACATCGTGGCGAGATTGCGCGGGTACGCCGATGAGGTGGT

Clone Rv103

.....Rv103SP6.seq:.....

AATACTCAAGCTTTCCGGCGAAACGGACACATTGCGAATATTGATGACAAAATAAAAATCATTGATGGTTTGAGTCAC
CAGGCCGATCAAGCCTTCGCCGAGCCAAATTCGAATCAAGAGGCCCAAGCCCGTACCAATCAGCCCGGCAACGAGGGA
TTCCGTCATTATCAGCCAAAATAACTGCTCTCGGGTTACCCCAAACAGCGCAATATGGCGAAAACGGTCCGCCGTTG
CACGACATTAAATGTCACGGTATTGTAGATTAAAAAGATACCCAC

.....Rv103T7.seq:.....

TGCTCCCGAAACCTGGGGGTGTGCCTGCTCTGTATGCACGGCATACGGACATCCTTCCCCTGAGACCCGCGGTGCAAC
CAGCCACGTGTCCATCATAGNGGGTCAACCCCGGCCAAGGGCGACGGCACGCCAAGTTCCGCCGACCGTTAACCTAGTG
CTGTTAGCTTCATTTGCTGCGATCAAAACAGCTGGTGGCCGTTAGGAAGTGAATTGAAACTCAACCGATTGGTGCC
GCCGTAGGTGTCCTGGCTGCGGGTGCCTGGTGTGTCGCGCTGTGGTAACGACGACAATGTGACCGGGGGAGGTGCA
ACCACTGGCCAGGCGTCCGGCAAAGTTCGATTGCGGGGGGAAGAAGACACTCAAAGCCAGTGGGT

Clone Rv104

:::Rv104SP6.seq:::

ATACTCAAGCTTTGCCGACGAGCGGGCGATGTTGATGACGGGAAACCCAGCGCACACCGACGATTTTGGCGTAGCC
GGCGGACGTCTGCTCGATTCCGATCACGTCCGGCGCTCGCATCGAGCATGGCGCCGGCGACGGCTAGCAGCGATCCGCC
GTCGTCGAGGAGCACGACACGAGCCGTACGCCCCGGCCGTAAGCCGCGCCAGGATTCGGCGAAAAACCGTTCTACGTG
GCGGGTGTACTGGGTGTCGAATGATTCTGTTGGGTGCGTAGGCGTCGCTGCAATCGTCGACATAGATGCCGTGGGCCG
CATCGCTCGACAACTCCGGGTGAGTGAATAGCACTTGCCGATCACCGCGACGTTGCGCGGATGAGGCCGAACCCGA
ATA

:::Rv104T7.seq:::

TCCTATGTCCCTGCCGAGCANGTGATCGAACGCGGTGACAGATTTGTCTATCCTGGACCTGACGGTGAGGTCTGAAGTT
TTCCAGGAATTCGGCAAAATCGGTAAGAGCCTGAAGAATTCGGTATCGCCGGACGAAATCTGCGACGCATACGGGGC
ATATACGCTTCGGGTTTACGAGATGTCGATGGGGCCGCTGGAGGCTTCACGTCCATGGGCCACAAAGGATGTTGTCGG
CGCGTACCGTTTTCTGCAGCGGTGTGGCGCTTGGTCG

Clone Rv105

:::Rv105SP6.seq:::

ATACTCAAGCTTGATTCCGCCGAAACCGACCGTGAGCACCCCGCCAGCCACCACGCTCGGGTCGGGCGCCGGGCCCGG
GCCGCCAGGCTGCTCCGCTCGGTGATGGCAGCCACCGCGACACCACCGGCTGCGCTACGTCTAACCATTCAGGCG
GAGCTACATCAGCTCGGCCGCCAGTGTTCCGGGCCCTCTTTCCAGGTCTAAGTCTATACCGATATGCGCATCCGCAGC
CGCCACCTGGAGAACAGAACGATGCCCTACTAATGCTTGCTGCGGGGCC

:::Rv105T7.seq:::

GGTACGCTTCGGTTCGAGTCTGCGAGTGATGCATGACGACCGGGACCTCGTCGGCATCTTCCATAGCCCGCCACACCT
TCAGTTGCTCACCGGAATCCAACCGGTAGAAGGTGCGCGAGCGCTCGGCATTGGTCATCGGGATATGCCGCTCGGGAC
GGTCAGAGCCCTCGGGTCCGGCCAGCACTCCGCAGGCTTCGTCGGGGTGGTCGCGACGCGCATGGGCCACCATCGCAT
TCACCAGGTCTGCGCGAATCACCAGCAGTAGACGGTTCTTTCTAAGCAACACCGAAGTTTCAGGACCCGAATGCT
CCGGGAAACATGTCACGGTAGGTGCGGTATTCCGGCTACCGGCTGA

Clone Rv106

:::Rv106SP6.seq:::

GGCGTCAACGGTGTCCGAACCCGCGTCAAGCAATTGGTAGGCCTGCAGTCTGTGAATCAGGCCGACGCTGTGGCCGCC
GCGG

:::Rv106T7.seq:::

GGCTNGCGTACCGGTACCGGCCGCGGGCCTACCACGTGCCGGAAGTGAAGCGCAGTAAGCCCTCAACGCGCCACCG
CTTTGGCCCGCGCGCCCGGCGTAGGCGCATCGGCGGTGGCGTGGGGCGGCGCACTGCGACCTCACCAGCGGCTTTTCG
AGCTTTGTTTCGATCAACCGCCAGCATGGTCGANGATGCATTTCGAGACCATATTGAAATTTGTTTCATCGGGGGCCC
CGATCCGATGCCCCCTCCAGTTGCGTGAGCAANCAGCGGAGTCNTCGCGGGATCGATGGCCACGGGGTGTTCATG
CGGATGTTCCGCTGCCCGCCGACTGGCTCTTGCGGGAGAACCGATCTAGCACACCGATCCGCGCACGTNG

Clone Rv107

:::Rv107T7D4.seq:::

CGTAATNTCGCGCACANCCANGACTTCTGGGGGGATCNGCTGACAGTGGTNGGATCCCAAATTGCGGATGATCGGGCC
GCCNACGTCGTTGTGTACCTCNCNCTCACAACNAANCCGAANCGTATGACTCGGTCCACGCGGTGCGGCACATGGTG
GACACCACACCGCCACCGCNCGGGTGAAGGCCTATGTACCGGTCCGGCAACACTCAATGCCGACCAGGCCGANGCC
GGACACNANAGTATCNCCTAACGTACCGCGATCACGAGCATGGTGATCGNNCAATGTTNCTANTGATCTATCGCTCCG
TAATTACCGCGTTCTCGTCTTGATCATGGTCGCANCGAACTCCGGCGCAATCCGCGGATTCATCGNCTTGCTCGCCG
ATCACATATTTTCAGCCTTTCACATTGCAACNAACCTGCTCGTCTCATGGNGATGCGGCGACACGGACTACCGATATC
ATGCTCGCCGTTACACAATCNCGCCACGCCGCGAAGACNGGAAACGCTTCTACACAATNTTNCGGGACGCCACTNAA
CTTGTTTCNGGTTTGACATTGCCGCGCATGTNTGCCAGCTTTGCCGGCTCCCCTTA

Clone Rv108

:::Rv108T7D4.seq:::

TGAATTTCCCGATCCCAATCTCGGTTTCAGATACAGGTGCGCCATACCCCTTACTTCGGCAACGCTGGGCGGATTGGC
CCTGCNCTGCAGCANACCATCGAGCCATCGAATTGCCGGCAATCTCGTTCAGCCAATCCATACCCATCGACATTCC
GCCGATCGACATCCCGGCCCTTCNCCCTTTAACGG

Clone Rv109

.....Rv109SP6.seq:.....
AACAGCTATGACCATGNTTACGCCAAGCTATTTAGGTAACACTATANAATACTCAAGCTTTTACGGTGATCGCGCATC
ACCTGGTTCATGAACTGGAAGCAGCGCANCCTTCCTTTTCGGCCGCAACATGAGCCAGCCTCTCGTCCGCGGTCTNGG
TGCAGGTGCTCGGGCAGCTCGGCCGCGACAGCCGCTGACCCTGAAACCAGCTTCCATATCCCGCGACNAACNACNCC
AGTCCGCTACGTAACCCCTCCGCGACTGTCCATGGACAACAGCGCGTTCTCCACCGACCGGGCCCGGGTGTGGGGTGT
TTCGGCGACCGGCAGGTGGTCCACACTGCCGCGCGGATTATCANGACTGACCTCCTGGCTGACCGGNTGTNTG
CCGCCCCGATCGCATACTCCAACCGGTTGCGGTACTGCAGGTGAGCTGGCGTACCTCCTCNCCTCGGCGAAGTCT
TGCTCCANCACGTGCGAGAACGGCAAGGAACACGTTCA

.....Rv109T7.seq:.....
GACCGNNCCATGTTTCCACAATGTGGTGCCAGTNCGGNGGCTACGTGCCATCNANACACTGGCGCAGGCTATCGCACC
CGTTATCNGCTACGAACAAATCNCGGTATGCGTCTTTTANCATGAGTCGGCGACCGNCGATCATGGTCGACACCCACG
ACNGAAATACGCAGATCGCCNTCNAGCNTGTGTGCCGCGGATTATCANGACTGACCTCCTGGCTGACCGGNTGTNTG
GTGCGGATGCCTGGCGCCCGGCGGCGTGTGCGTGGTGGCTCGGATAGCGAAGTCAGCTAATTCTCGTGGCAGCTCG
AAAGGGTCTGCGCGGTGCGGCTCTTTGCGCAAACCATGCNCATGTTACGGTCCCTCGGGTGGCGCCTGGCGGCGGC

Clone Rv10

.....Rv10SP6D2.seq:.....
GGGATGGGCGGGCCCGCTAAACTCTTCGTGTTCCACTAACTCCGGGAGGGNCAATCTCGGGCCGTTATGGCTCACGTC
CGCTCGCCCTCCGACCGCGAACATTGCGAGTTGGCAGCAACCTGGTAGCACCTGGCCGG

.....Rv10T7D4.seq:.....
NCCGTCGTTGACAAGTAAATATGTCCGCAAAAGTCTCAGCGGCCGACTTTGCTCGCAGGTGGCGGTACCGCGCCACCG
AGTCGATGCCGTGGTTCGCGGAAGAATGCCTCCCGAAATCGCACGGCCTTCCNNTTTAAACGGA

Clone Rv110

.....Rv110SP6.seq:.....
TTTAGGTGACACTATAGAATACTCAAGCTTTTGGTCTAGCCGGCCGAGCACGATACGGGTGTCAATTGGCCACCGGCGG
CGGCTGTCCGGGAAATGGCGGGTCCCCGGTGGTTTTGTCTGATGAGTGCTGAACCGTANTCGAAGTGGGCGGCGTCAGA
CTCCACCCANCCAGCAGCGAGCGCAAGCTGAATCCTCCAACCGGTTGTGNATCCGGACAAGTTGGGGTGCGTTTGG
GGCAATGACAGGTGGCNGCGGTGCGTTTCGGGTCCGCCGGCGGAAGTGCTGCGTTGGGATCNCCTGCTGGGCATTTCGGC
NTTTTTCGGGCGGCGGTGGTNGGGGGGCAACAGGTNTCCNNGTGGGGTGGCGCTCAACGGTCNACGGCGCAAGCCG
CCGTTGTTGGTACNNGGGGCGCTGGCTCCGGATCGCGTTGGCGGTCNCCGG

.....Rv110T7.seq:.....
CTACACCATCGAATACGACGGCTCGCCNACTTTCCGCGGTACCCGCTCAACTTTGTGTGACCCCTCAACGCCATTGC
CGGCACCTACTACGTGCATCCAACTACTTTCATCTGACGCCGAACAAATTGACGCAGCGGTTCCGCTGACCAATAC
GGTCGGTCCCACGATGACCCAGTACTACATCATTCGCACGGANAACCTGCCGCTGCTAGAGCCACTGCGATCGGTGCC
GATCGTGGGGAACCCACTGGCGAACCTGGTTCAACCAAACCTGAANGTGATTGTTAACCTGGGCTACNGCGACCCGGC
CTATGGTTATTTCNACCTCNCGCCCAATGTTGCGACTCCGTTCCGGTGTTCCTCCANAAGTCNNCCCGGTGTCATCGC
CGAANCTCTCNCCTCCGGGACCCACAGGAATCNGCNATTTNCCTACAAATCANCCACCTCCA

Clone Rv111

.....Rv111T7.seq:.....
GCATGATCGGCCACCTTTTCGGGCGCCCGGCATACGGCGGCGTACCGATCTCCGCGTCATACACCCGCGGGTAATCGC
CGACGGTGCCGGTTCGCGAGCCGAAGGTGACGACTCTGATTGAATCGAGTTCAGGTCCAGCGGGTGGCGCACCAACG
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Clone Rv112

.....Rv112SP6.seq:.....
GACACTATAGAATACTCAAGCTTGCCAACCGCCAGCCTGCATCCGGCGGCGANCACTGCTCCGCCGACAGTACGAAC
CAACCTGCGGTGCCAGGCCATTGACGATGTGCTGGTCGGCGCCCGCGAGTCCGCGCACCATCAACGCCGCGGGCACC
ACCANGGCGGCCCCACCCTGCACGGCGACGATCATTCGGCGCCGCTCACGGCGGGCGGGGCTCGAACANGCACAGCA
TCAACGTNGTCACCCGGCCGTGACCGGCCCGCATCGTCACACCACCCAAGCCATTGCCGTCTCTCAACNNGGGCGA
CCCGGCCCGCATCGTCACACGGNCTAAGGCCATTGCCGTCTCTCT

.....Rv112T7.seq:.....

TCGGCGCCATCGGCACCTTCGAGGACCTGTATTTTCGACGCCGTGGCCNACCTGAGGTTGGCGGTGGACNAAGTGTGCA
CCCGGTTGATTTCGCTCGGCCCTTGCCGGATGCCACCCNGCGCCTGGTGGTTCGATCCGCNAANAGACAANTTGTGGTGGA
NGCTTCTGCTGCCTGCGACACCCACNACGTGGTGGCACCGGGCAGCTTTAGCTGGCATGTCCTGACCGCGCTGGCCGA
CNACTCCAGACNTTCCACNAANGTTCGCCNNCCCAATGTNCCGNANTGTCTCCGGNTCCCTTTACCNCCCAATGGGCN
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Clone Rv113

.....Rv113SP6.seq:.....
ATACTCAAGCTTTTATGGTGATCGCGCATCACCTGGTTCATGAACTGGAAGCAGCGCAGCGCTTCCTTTTCGGCCGCA
ACATGAGCCAGCCTCTCGTCGGCGGTTCGGGTGCAGGTGCTCGGGCAGCTCGGCCGCGAACAGCCCCGGCTTGAACCCGTG
AAAACNGCTTTCCATATCCCGCGACGAAAGAACGCCAGTTCGGCTACTTAACCCCTCCGCGAACCGTCCATGGACAA
CAGCGCGTTCTCCACCAACCGGGCCCCGGGTGT

.....Rv113T7.seq:.....

TCGGCTCAGGCCGCGCTGCTGGTAGAGTCGCTGACCGGTGCAGGTTTCGACAATGTGGTGCCGGTTTCGGCGGCTACGT
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GTCGGCGACCGTCGTTCATGGTCGACACCCACGACGGAAAGACGCAGATCGCCGTCAAGCATGTGTGCCGCGGATTATC
AGGACTGACCTCCTGGCTGACCGGCATGTTTGGTTCGCGATGCCCTGGCGCCCCGGCGGGCGTGGTTCGTGGTTCGGCTCGGA
TAGCGAGGTACGCGAATTCTCGTGCGAGCTCGAAAGGGTCTGCCGGTGCCGGTCTTTGCGCAAACAATAGCGCAGGT
TACGGTTCGCGCGGGGTGCGGCCTGCGCGCGGCC

Clone Rv114

.....Rv114SP6.seq:.....
CAAGCTATTTAGGTGACACTATAGAATACTCAAGCTTCGCGTCTACGCCGGCCCCGAGCATCCGCACAGCGCTCAGCA
GCCGGTTCCGTACGANCTCAAGCAGGTGGCGCAATGACCGAAACCACCCAGCCCCGCAAACCCCGCGGCCCGGCC
GGGCCCCGACAATCGTTTCGTGTTGGAGCGGCCCATCCANACCGTTGGGCGCCGTAAGGANGCCGTGGTACGAATGCGG
CTGGTCCCCGGCACCGGCAAGTTCGACCTCAACGGCCGCAGCTTGGANGACTACTTCCCAAACAAGGTGCACCAGCAG
TTGATCAAGGCACCCCTGGTCAACCGTGGATCGGGTGGAAAGTTTCGACATCTTTGCCACCTGGGCGGGCGGCCGT
CCGGTCAGGCCGGGCTGCCCTGGGTATCGCCGGGCATTGATTCTGGTATCCCNAGAAGAACCG

.....Rv114T7.seq:.....

CGGTTGGCCACCGCTTCTGCGGTGCCGCCGCGTCGACAATGACCGTGTCTGCTCCTTGCTGACCACCACGCGTCGGGCC
GAGCCCAGCACCTCCAAGCCACCTCGCGCAGCACCATGCCGGCGTCGGGGTTGACCACCTGGCCACCCGTCAACACC
GCCAGGTCTCAAGGAAACGCCTTACGGCGGTACCCGAAGTACGGCCCCCTTGACCGCGACCGCTTTCAACGTCTTGCG
AATCGCGTTGACGACCAGCGTCGCCAACGCTTCGCCCTCCACGTCTTCAGCCACGATCAGTAGTGCTTACCCGTTC
TGCAACCTTTTCCAGCAATGGCAACAGATCGGGAAGCGANCTGATCTTGTCTTGGTGCN

Clone Rv115

.....Rv115SP6.seq:.....
CCAAGCTATTTAGGTGACACTATAGAATACTCAAGCTTTTGGCTGGGTGCGCTTCGAATTCNGCGTGCACCGCTATGG
GTTGCANAGCGGCTGGCGCCGCACACCCCACTGGCCCCGGGTGTTTCGCCCCGAACCCGGATCATGGTGAGCGAAAA
GGANATTCNCCTGTTTCGATGCTGGGATTCGCCACGCCAAGGCATCTANCGATTACTCTCCNCGGGGTGGGAAAAGTGC
CCAATCCCCCTCCCTCCAACCTTTCNAACAATCATTCGGGTTCCNCCNTCCGGTTGGNGGTAACCNCCAAATAAAACC
CCTGCCCG

.....Rv115T7.seq:.....

GCCCCNCATGGCCAATCCCCGAAGACATCATTTGGCCAGTGGCCGGGCGCTAACAGGTTCCAGCCCCCACCANTGCC
GCTCGAATATGCGGTGCAACCCATTCGACGGCCGGCAGGGAAAGCACCAGCGGAAGCCGCAAAGGGCTGCAGTTCCGCG
CCCAATAATGTGCTCCGCAACCATGCGCTCNAAAACCNCCGGCAGTCAGCGCACCCGCGANGTCGAAAGAC
GTNCTCAGCGCGCCACATGGGGTGCCAATCGGCACGGCAGGTATGCCGCGCGCAACCCGAGCGCGTGGTGCATGCC
ACGGTCCGCANGANGCGCANACCCGCCAATGCCGAANCCACGAAACATCGGGCGCATCCACCTTCAACC

Clone Rv116

.....Rv116SP6.seq:.....
ATACTCAAGCTTGGCCAGCCGTTCGATGACAAGAAATATGTCGCAAAAGACTCAGCGGCCGACTTTGCTCGCAGCTGG
CGGTACCGCGCCACCGAGTCGATGCCGTGGTTCGCGGAAGAATGCCTCCCGAATTCGCACGGCCAATTCCATTCCGGGA
AGCATCCGCAATGCCAGCTGCGGTTGCCCCCTGCCGGCCACGGCACCCACTTGCGGCATTGCGTCCACCTGGGCCAGC
GCCCCGCCGCAATTCCAAACAATAAAAATTGCACCCGGC

.....Rv116T7.seq:.....
CCACCCGTGTATTTTGGGATGGGCAAAAAGGCGAAGCACCGCGTGGCCACGAACGCCGGGAGGGACAATCTCGGGCGG
CTAGGGCTTCTCGCGGGAAGGCCCCGAACGTACGGCGTTTCAACACGTGCGCTCGCCCTCCGACCGCGAACATTCTGGGG
ATGGCAGCAACCTGGTAGCACCTGGCCGGGCGATGATCTGCAGCGTCGCCGCGGGTAGTCGCCGCCCGGGCGGCTAC
AGTCTGAAACGCGATGACCATCGATGTGTGGATGCAGCATCCGACGCAACGGTTCCTACACGGCGATATGTTTCGCTC
CCTGCCCCGT

Clone Rv117

.....Rv117SP6D2.seq:.....
CTGCCCATGTTTGGGGACGCCCCGACCAGCCGATGCTGGAGGCCTACACGGCCCTTGGTGCGCTGGCCACGGCGACCGA
GCGGCTGCAACTGGGCGCGTTGGTGACCGGCAATACCTACCGCAGCCNGACCCCTNTCNCAANAGGATNTTGTTCGCC
GGACCCCNCTC

.....Rv117T7D4.seq:.....
CCGACTTTCGCGGTACCCGCTCAACTTTGTGTGACCCCTCAACGCCATTGCCGGCACCTACTACGTGCACTCCA
ACTTCATCCTGACGCCGGAACAAATTGACGCAGCGGTTCCGCTGACCAATACGGTTCGGTCCCACGATGACCCAGTACT
ACATCATTCGCACGGAGAACCTGCCGCTGCTAGAGCCACTGCGATCGGTGCCGATCGTGGGGAACCCACTGGCGAACC
TGGTCAACCAAACTTGAAGGTGATTGTTAACCTGGGCTACGCGACCGCCTT

Clone Rv118

.....Rv118SP6.seq:.....
ATACTCAAGCTTTGTACACCAAGTGTTCGACCAGGCGCTCCATCCGGCGAGTGGATACTCCCAGCAGGTAGCAGGT
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CAGCTGGGGGATCCCAACTTCAATGGTTGCGGCACGGGTGTCAAATTACGGTGCGGTTAGCCGTTGCCCTAATTGGA
CCGCTCATCGTGTTCGCGGTACCCCGCCCCGCACAGGGCTTCGGCTTCAGCCCCCATCAGGGCGGCAATAAACTT
CAAGAGCACC

.....Rv118T7.seq:.....
GAGGCAGCTTCGCCGGCAATTCTACTAGCGAGAAGTCTGGCCCGATACGGATCTGACCGAAGTCGCTGCGGTGCAGCC
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TCAAGTCCGCTTACGCTTGGGCTTTGCGGACGGTCCCGACGCTGGTTCGCGGTTGCGCCGCGAAAGCGGCGGGTTCGG
GTGCCATCAGGAATGCCTCACCGCCGCGGCACTGCACGGCCAGTGCCGCGGCGATGTACGCCATCGGGACATCATGCT
CGCGTTCATACTCCTCGACCACTCGGCGGAACAGCTCGATTCCCGGACCGCCAGCGCATTGGTGATGGAATCGGCGA
ACTTGGCCACCCGCTGGGTGTTGACATCCTCGACGGTGGGCAATTGCGCCTCGGTAAGCTTTGCCGCGTAGCCTTTTC
ATC

Clone Rv119

.....Rv119SP6.seq:.....
ATACTCAAGCTTCACTGACAAGGGACGAATTCGTGCGCCGCTGTTGACTGGGTGGTGGCCGAGCTGGTCCGCCACCA
CTCAGGCCGCGGTACGCGCGGTACCGGCGCGGGAGCAAATCGCGCGGGCATGGCCAATTCTTGCGGACCATCACCG
CAGACGCCCCGCTTCGGACCCCTGCTGTCCACCACACAGTTGGCCAACGCATTAATACCCCGCAAGCTTTCGGGAATCCA
CCGCCCTGTTTCG

.....Rv119T7.seq:.....
TCCATCACCCGATGTGGCNGGAGCACTGCCATGTCGATCTCAACTACCACCTCCGGCCGTGGCGGTTGCGCGCCCCGG
GGGGTCCGCGCGAACTCGACGAGGCGGTTCGGAGAAATCGCCANACCCCGCTGAACCGCGACCAACCGCTGTGGGAGA
TGTAATTCTGTTGAGGGGCTTGCCAACCACCGGATCGCGGTGGTTGCCAAAATTACCATGCGTTGGCTGACGGTGTG
CCTCGGCAAAACATGATGGCACGGGGGATGGATCTGCCGCGGGGACCGGAGGTTCGGCCGCTATGTGCTGACCCCGCTC
CTACCAAGCGGCA

Clone Rv11

.....Rv11SP6.seq:.....
AGCTTTGCAGTTGCTGAGTAATGTCGGCCAACGTACACACAACCGCGATGAATTCAATCATGCCGCCAGGGCGGCCA
ACCCAATGGTGGCCGCGAGCGGCAGCTCGATCGCAGCGCGGAGGTTGCCGGCCGCGAGTTGATTACGGAACAGGGTGA
GGTCATAGGCGGGCAGGATAGTGACGAAGGCAAGACCTCCATCTGCCGTCGGAAGAAGTATCGAG

.....Rv11T7.seq:.....

AGCTTCAGAACAGGCCTGTTGTGGGCGCACCCGGCTCGCCGAGTTCTGCACGCACCGCCTCAAGTGCGGCCCCGCACCG
CCGGCATCTCCCGGTACAGCAGGGCCGCGGCCCGCGCCGACGCGACGGCGTGTTGCGCGAGTTCGCCGTCAATGATGC
TGACCTGATCGGCCACCCGGGCGTTCTCGGCGTCTGTCGCTTCACTAATCGCGGTGCTCAGCAGCGTCTCGACAGCCA
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Clone Rv120

.....Rv120SP6.seq:.....

ATACTCAAGCTTCAGTTCCTCCACGACGCGTTCCTCAAATGAATTTCCCGATCCCACAATCTCGGTTTCAAGATACAGGTC
GCCATACCCCTTACTTCGGCAACGCTGGGCGGATTGGCCCTGCCGCTGCACCAAACCATCAACGCCTTCAAATTGCCG
GCAATCTCGTTTCAAGCAATCCAT

.....Rv120T7.seq:.....

GCTCTACGCCGCTACGGGTGCAACATGCATCCCGAGCAGATGCTCGAGCGCGCACCCCACTCGCCGATGGCCGGAAC
CGGCTGTTTACCCGGGTGGCGGCTGACGTTTGGCGGCGAGGACATCNGCTGGGAAGGGGCGCTTGCCACCGTCTGTCNA
AGACCCAAATTCGAAGGTGTTCTGTCGTCTTACGACATGACCCCGGCGGACGAGAAGAACCTTGACCGGTGGGAAGG
CTCCGAGTTTGGTATCCACCAGAAGATCCGATGCCGCGTGGAGCGCATTTCTCGGACACCACAACGGGATCCCGTCC
TCG

Clone Rv121

.....Rv121SP6.seq:.....

ATACTCAAGCTTGCCAAAGAGACCTCGTCCACCAAGCAGGACGCGACCGTCGAGGTGGCGATCCGGCTTGGCGTTCGAC
CCGCGTAAGGCAAACAGATGGTTTGGCGGCGACGGTCAACCTGCCACACCGGCACTGGTTAAGAACTGCCCGCGTCCG
GGTTTTTCGCGGTTGGTGAAAAGGCCAATGCCTGCGTTTGCCGTGGGGCGGATGTTGTGCGGAGTGACAATCTGATCA
AAAGGATTCAGGGCGGTTGGCTGGAATTCAATGCCGCAATCGCGACACCGG

.....Rv121T7.seq:.....

CCACGGCGTGGATCAAGGTACCGGCCGGGATGTTGCGCAATGGCAGGTTGTTGCCCGGCTTGATGTGCGCGTTAGCGC
CGGATTCACCATATCCCTTGGCAAAGTCCGTTGGGTGCAATGATGTAGCGCTTCTCCCCATCGAGATAGTGGAGCA
ACGCAATCCGTGCGGTACGGTTTGGGTGCTACTCGATGTGCGCGACCTTGGCGTTGACACCATCTTTGTATTGCGGC
GAAAGTCGATCATCCGTAAGCGCGCTTATGACCGCCGCTTTGTGCGGTTGGTAATCCGGCCATGCGCGTTGCGTC
CACCGCGACGTGCAGCGGGCGCACACGCGACTTCTCCGGGGTTGACCGGGTNATCTC

Clone Rv122

.....Rv122SP6D2.seq:.....

GCAGCATGACGGCGGTAGCGAACACCGCCGGATGCAGCGCAAGTAGCGTCGATGTGCTCACGGAATCGCCCCGGCACC
GCGATCTCGANGATCACCAGTGCCACCCCCCTGCAGCGCNACACCGACGATTCCGTACACCGCCACGCCGATCAGGCCC
TGGGCCATCTGATTGGAGCTGGCGTANATGGCGGCGATGGTGACGATGGCCAGCGCCACATACATTGTGGCGGCCAGA
ACCACGGCGTTGGGGCGGCGGTCGATGAACACTAGGCGACGCGATCGCCCGGGTCAACAGGTTGACCATCAGAAAG
CCTGCGACTAGCACGGCGGCGCCACTAGGAAGTACAAGAANGTGGCCACCACCCCATGCAGGATCGGGGTAAGGCTGA
TGGTCCCGAAATCGACTCCGGCCTAATACATGACTCTCTCTTTCGCTCATCGCCTTACTTGTGCGCGGAA

Clone Rv

.....Rv123SP6D2.seq:.....

GGGACACACCTCGATGCTGCCGCNATGGACGCGGTGCAACGCAAGCAGCTGATCGAGCTACAACGCCGCGCGGAACGC
TTCCGCCGCGGGCGTGACGCATCCCGTTGACCGGCCGGANCTCTCTA

.....Rv123T7D4.seq:.....

TGGGCGCCTCTTTGCGCCTTCCNNTTTAAACGNAGCANGACATTCTGGGTATCGAGTTGTACTGGATGGTGTGGCG
ATGTGCGTGATCTGCTCTTGGCGGTGGGATCCGACTACAATCTGCTGCTGATTTCCCGGTTGAAAGAGGAAATTGGG
GCCGATTGAACACCGGAATTATCCGTGCCATGGCTGGTACCAGGGGAGTGGTGACGGCTGCCGGCATGGTGTTCGCC
GTTACCATGTCGTTGTTTGTGTTTCAAGCATTTGCGAATTATTGGTCAGATCGGTACCACCATCGCCTTCCC

Clone Rv124

.....Rv124SP6D2.seq:.....

CCGATCGGCGCCGCANCTGGTTGGTGTTCGGATGAATCCGCAGCGAAAATGTAGCTGCGGTGGCGTGTGCTGACTCG
TNGGCGTCGACGCTCGTGGCAGCCACCGANCGGTTGGTCCAGGATCTGGATGGGCAAAGTTGTGCGGCCCGGCCGGTG

ACGGCCGATGAGCTGACCGAGGTGACAGCGCCGTGTTGGCTGACTTGGAACCGACATGGAGTCGCCCCGGTTGGCGT
CACCTCAAGCATTTCATGTTATGCGACCAAGTTTGGGTTACGCCGTGACACATCACGTCGGAGACTTGGATGAGC
TGTGTCTGCCAGATAGCCCCGAATCGGGACGACCGTGGTCACGGTGCGTCTGACCACTCGGGTCGGGTCGCCCCGCGT
ATCGGCATGGGTGCGTNATCACAGCGACACGCGCCTGCCAAGGANGTNCGGNCGGACC

::::::::::Rv124T7D4.seq::::::::::
CGGGTTGCGGATCCACGCGTGCGGGTTGTGACGAGCTACGGCACTGAACCGCGCCACAGCTCGCCGATCCGCTTTCCG
GTGGTTCTCGATCGACTCGCCGTAGGCGATGCGCAGCGCCTGCTCGAATATCGGGTACACGTAGGCCGGCCTTCCNC
TTTA

Clone Rv126

::::::::::Rv126SP6.seq::::::::::
CTTGATTTTGATCATCATGACGATCATACCCTAATTTTGTCTACCCGCACTGGTTATCGTGGGTACCGTCGTGCTTTC
GAGCGGGACACACCTCGATGCTGCCGCCATGGACGCGGTGGAACGCAAGCAGCTGATCGAGCTACAACGCCGCGCGG
AACGCTTCCGCCGCGGGCGTGACCGCATCCCGTTGACCGGGCGGATCGCGGTGATCGTCGATGACGGCATCGCCACCG
GAGCNACTGTCAAGGCGGCGTGCCAGGTGCGCCGGGCGCACGGTGCGGACAAGGTGGTGTGGCGGTCCCGATCGGCC
CAGACGACATCGTGGCGAGATTCGNCGGGTACGCCGATGAGGTGGTGTGTTTGGCGACGCCGGCGTNGTTCTTCGCCG
NCGGGCANGGTTACCGCAACTTCAACCAGACCTCCGACGACGAGGTGGTGGCGTCTCCTGGATCGTGCTC

::::::::::Rv126T7.seq::::::::::
GGGGATCCCTAGATCGACCTGCAGGCATGCAAGCTTGGCGTGTGCTTCCAACCCGAATTGGCTTTCGGCGCCATCGGT
GAGCGGGACACACCTCGATGCTGCCGCCATGGACGCGGTGGAACGCAAGCAGCTGATCGAGCTACAACGCCGCGCGG
AACGCTTCCGCCGCGGGCGTGACCGCATCCCGTTGACCGGGCGGATCGCGGTGATCGTCGATGACGGCATCGCCACCG
GAGCNACTGTCAAGGCGGCGTGCCAGGTGCGCCGGGCGCACGGTGCGGACAAGGTGGTGTGGCGGTCCCGATCGGCC
CAGACGACATCGTGGCGAGATTCGNCGGGTACGCCGATGAGGTGGTGTGTTTGGCGACGCCGGCGTNGTTCTTCGCCG
NCGGGCANGGTTACCGCAACTTCAACCAGACCTCCGACGACGAGGTGGTGGCGTCTCCTGGATCGTGCTC

Clone Rv127

::::::::::Rv127SP6.seq::::::::::
AAGGCTGCAGGTGCAAGCGGNTGGTTACGACTCCCTGTGTGTGATGGACCAAGTTCTACTATCTGCGTCTACACGGCCC
TTGGTGCGCTGGCCACGGCGACCGAGCGGTGCAACTGGGCGCGTTGGTGACCGGCAATACCTACCGCAGCCCCGACC
CTGCTGGCAAAGATNATCACACGCTCGACGTGGTTAGCGCCGGTCGAGCGATCCTCGGCATTGGAGCCGGCGGGTTT
GAACTGGAACACCGCCAGCTCGGCTTCGAGTCCGGCACTTCCAGTGACCGGTTCAACCGGCTCGA

::::::::::Rv127T7.seq::::::::::
CTTTCCGCGGTACCCGCTCAACTTTGTGTGACCCCTCAACGCCATTGCCGGCACCTACTACGTGCACTCCAATACTT
CATCCTGACGCCGGAACAAATTGACGCNCGGTTCCGCTGACCAATACGGTCGGTCCCACGATGACCCAGTACTACAT
CATTTCGACCGGAGAACCTGCCGCTGCTACAGCCACTGCGATCGGTGCCGATCGTGGGGAACCCACTGGCGAACCTGGT
TCAACCAAACCTGAAGGTGATTGTTAACCTGGGCTACGGCGACCCGGCCTATGGTTATTTCGACCTCGCCGNCCAATGT
TGCGACTCCGTTCCGGTTGTTCCAGANGTCAGCCCGGTGTCATCGCCGACGCTCTCGTCN

Clone Rv128

::::::::::Rv128SP6.seq::::::::::
CGGTCATAGCCCTCGGGTCCGGCCAGCACTCCGCAGGCTTCGTGCGGGTGGTTCGCGACGCGCATGGGCCACCATCGCA
TTCACCAGGTCTGCGCGAATCACACGACGTAGACGGTTCCCTTTCCTAAGCAACACCGAAGTTTCACGACCCGAATGC
TCCGGGAACATGTCACGGTAGGTGCGTATTCGGGCTACCGGCTGAGCATTGAGCAGCCGGCCAGCACCGCACGAGC
CAGGCAATCAGCCGCCCGCCGACCGATCGCGGTGACCACTGAGTCTCCGGAGACAATGCGGCGCGGCACGCCGGNCTC
CGGCGGCACCGCTACNGCGCCCGTGG

::::::::::Rv128T7.seq::::::::::
GTGATGGCACGCCACCGCGACACCACCGGCTGCGCTAQTTCGAGCCATACCGGGCGGAGCTACATCGGCTCGGCCG
CCAGTGTTCCGGCCCTCTTTCGAGGTGCGAGTTCGATACCGATTTCGCGCATCCGCANCCGCNCCCTGGACGACAGAACC
GTGCCCTACGAGTGCTTGTGCGGCGGGGCCAAAGAACAGCTTGGCATCCTGGCGGATGGCCGGCGCGGCGTGGTC
GCCAAGGACGACGCCGTTCCGGTGCTGATCGACGACGCGTGGGGTTACCGATCCGGAGCGATCAAGATGGGGG
AGGTCTCTGACACCATCGGCCCNACGGACATGTGATCGTGCGGACGTGCAGTCCCACCCG

Clone Rv129

::::::::::Rv129SP6.seq::::::::::
GCGAAAGTCCGTTGGGTGCAATGATGTAGCGCTTCTCCCATCGAGATAGTGAGCAACGCAATCCGTGCGGTACGGT
TCGGGTCTGACTCGATGTGCGCGACCTTGGCGTTGACACCATCTTTGTATTGCGGCGAAAGTCGATCATCCGGTNNG

CGCGCTTATGACCGCCGCTTTGTGCCGGGTGGTAATCCGGCCATGCGCGTTGCGTCCACCGCGACCGTGCAGCGGGC
GCACCAGCGACTTCTCCGGGGTTGACCGGGTGATCTCGGCGAAATCAGATACGCTGGCGCCGCGACGACCAGGCGTGC
TGGGCTTGTNCTTGCGAATTGNCATGTCTAATCANGTCTTCTCTCACGCTCTCGTCCGCCGGGCTAGGCCGATTGCC
CTGCTCCTCCTCATCGCTTCGCTCTGCATCGTCCCCGGGCTAAGCCCGTGCCCCGAA

::::::::::Rv129T7.seq::::::::::
GATGGTTCGCGGCACGGTCAACCTGCCACACGGCACTGGTAAGACTGCCCGCGTTCGCGGTATTTCGCGGTTGGTGAAAA
GGCCGATGCTGCCGTTGCCCGGGGGCGGATGTTGTCCGGAGTGACGATCTGATCGAGAGGATTTCAGGGCGGCTGGCT
GGAATTCGATGCCGCGATCGCGAACACCGGATCAGAATGGCCAAAGTCGGTCGCATCGCTCGGGTGCTGGGTCCGCGC
GGCCTGATGCCCAACCCGAAAACCGGCACCGTCACCGCCGACTCCCCATGGCGTCCCGGATATCAAGGGCCGGCAAAT
CAACTTCCCGGTTGATCAGCAAGGCAACCTGCCTCCNCTCCGG

Clone Rv130

::::::::::Rv130SP6.seq::::::::::
ATACTCAAGCTTCGTATAAGACCATGGTGCGCTTTCTTTACCCGTCAGAGTCGGGGGCATCCGCACCGGCTCGCA
TCGCATCATCCTCCCACGACGGGCGGCTCATCAGCTTGGGCCATTTCAATGTAATTGATACCCCGCGCTGCGGGTAGG
CCACTGCGACAATTCAAACACGGTGTACACGGTGAATAGTGTGAGATGGGCTCTGATCAACCGTCGCAAACCCGGT
TTCGCATCAATAGCGGAATCCCACCGGTTGCATGGAGGCTGCTGACCTTGAAAACAAAATTTTTTCATTACAACAA
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Clone Rv132

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Clone Rv134

::::::::::Rv134SP6.seq::::::::::
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CAAGCTAGTTAGGTGACACTATACAATACTCAAGCTTACCGGCTGGTGGGCGGACCACTTCGATGGCAGCAGCCGTGA
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Clone Rv135

:::Rv135SP6.seq:::

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Clone Rv136

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Clone Rv137

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:::Rv137T7.seq:::

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Clone Rv138

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Clone Rv139

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Clone Rv13

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Clone Rv140

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Clone Rv141

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Clone Rv142

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Clone Rv143

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:::Rv143T7.seq:::

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Clone Rv144

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Clone Rv145

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Clone Rv146

:::Rv146SP6.seq:::

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CAACGCCGCGCGGAACGCTTCCGCCGCGGGCGTGACCGCATCCCGTTGACCGGGCGGATCGCGGTGATCGTCGATGAC
GGCATCGCCACCGGAGCGACGGCCAAGGCGGCGTGCCAGGTGCCCCGGGCGCACGGTGCGGACAACGTGGTGCTGGCG
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Clone Rv147

:::Rv147SP6.seq:::

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CAGCTTCCATATCCCGCGACGAACGACGCCAGTCCGCTACGTAACCCCTCCGCGACTGTCCATGGACAACAGCGCGTT
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:::Rv147T7.seq:::

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ACCCACGACGGAAGACGACGATCGCCGTCTANCNTGTGTGCCGCGGATTATCAGGACTGACCTCCTGGCTGACCGGC
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Clone Rv148

:::Rv148SP6.seq:::

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:::Rv148T7.seq:::

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Clone Rv149

:::Rv149SP6.seq:::

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Clone Rv14

:::Rv14SP6.seq:::

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:::Rv14T7.seq:::

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Clone Rv15

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:::Rv150T7.seq:::

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GTTGGCCGCCGCGGACGATCTTGGCGTCCACGGTGGTCCGGTCTTGCCCGCTAGCACGATCCGCGAGTCGGCCGG
TCACCCGGGT

Clone Rv151

:::Rv151SP6.seq:::

ATACTCAAGCTTTCCAAGTCCCAAGTGTGATCATGGCCAAAGAGCTCGACAAAGCCGTAGAGGCGTTTCGGACCCGC
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GGGGTGACACCTTGATCGCCACCGCGTCAACGCCGAGGGCTACCGAAAGATCCTGGGCATCCAGGTCACTCCGCC
GAAGACGGGGCCGGCTGGCTGGCGTTCTTCCGCGACCTGGTCCGCCGCGGCTGTCCGGGGTTCGCGCTGGTCAACAGC
GACGCCACGCCGGCCTGGTGGCCGCGATCGGGGCCACCTGCCCGCAGCGGCCTGGCAGCGT

:::Rv151T7.seq:::

CAGGCATGCAAGCTTCAACGTAGCGCGCTCGATAAATGACTCCGCCGCGCTTCGCACATCCTCGTAGCGATCCTTG
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AGCGAATCCGAGAGCAGGAGGACGAGGTACGAAGCTGCGCCAGCCGGTCTGACCGCTCAGGGCGGATGTCGCCGGTC
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Clone Rv152

.....Rv152SP6.seq:.....
CGCGGCGGCGCATTACCCCCGCTACCGTCAGCAGCTTGACGGCGGTAGCGAACACCGCCGGATGCAGCGCAGGTGCGT
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.....Rv152T7.seq:.....
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GGCGTCCACGGTGGTCGGGGTCATGCCCCGCGAGCAGGATCGGCGAGCGGCCGGTCAGCCGGGTGAAGTTCGTCGAGAG
CTTGACCCTGCCGTGCGGGAGGCGAACACGGTCGGTGCGTATCTCGACCAGGCCCGGGCAACCTCGGGGGTGGCGCC
GACGGTGAACAGGTTGCGCTGGCCACCGCGGGTAGCCGCCGGCACTATGCCGATGCCAGGCCGCGGATCACCGGTGC
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Clone Rv153

.....Rv153SP6.seq:.....
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GGTATATGACCTCGGTTTCTCGGGTGCTACCGCGTGCCCTGTGCGAGGATGAAGTTCGGCGTTGGAATTGTCCAGCCGGC
CCAATTCATCGAGCGCAGATTTCGTACACATGGCCGCGGCGACATACGCTTCACCGTGGATCTGCTCCACACGGACCG
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.....Rv153T7.seq:.....
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GGCTGCCGCTGCAGCGGTTGTTTTCCGAACGCATCGGGCTCGAAGACGTCGAGGAGGCGTTCACAAAGATGCATGGCG
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Clone Rv154

.....Rv154SP6.seq:.....
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GGTGTTCGCCGTTACCA

.....Rv154T7.seq:.....
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CCGCATCCCGTTGACCGGGCGGATCGCGGTGATCGTCGATGACGGCATCGCCACCGGAGCGACGGCCAAGGCGGCGTG
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Clone Rv155

.....Rv155SP6.seq:.....
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.....Rv155T7.seq:.....
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TGACGCCGGAACAAATTGACGCAGCGGTTCCGCTGACCAATACGGTCGGTCCCACGATGACCCAGTACTACATCATTC

GCACGGAGAACCTGCCGCTGCTAGAGCCACTGCGATCGGTGCCGATCGTGGGGAACCCACTGGCGAACCTGGTTCAAC
CAAACCTGAAGGTGATTGTTAACCTGGGCTACGGCGACCCGGCCTATGGTTATTCGACCTCGCCGCCCAATGTTGCGA
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Clone Rv156

:::Rv156SP6.seq:::

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AACCGTGGCCATCACNTCCGGGTGTCCACACCGGAGGACCCGGCGTCCGCCGGTTCGGCGAAACGTTGTGGGAGTTC
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:::Rv156T7.seq:::

TCGCCACCGCACCGCGGCGAACGCTCAAAGGCACCTACTGGCACCAAGGCCCCACACGTCACCTGTGACCTCCTGCG
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TGTCCGACGACTACACCAACCCAGGCCATCGCCGCGCGCCGCGATGCCAACTTCGACGCCGTACTGGCCCCGGCGG
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Clone Rv157

:::Rv157SP6.seq:::

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GGAACAACTCCAGGTAGAGGTACACACGCGGATAGCCAATTACAGAGTAATAAACTGTGACACTCACACCTCATCAAT
GATGACGAATAACCCCGATATCCGGTCACATGACGAAGGGAAGAGAAGGATATCATCTGTGACAACTGCCCTCA
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Clone Rv159

:::Rv159SP6.seq:::

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GACGGTACCGGAGGGCAGCGACAAAACACTTATGCACCTGGGCGACCCGCGAGACGGTGCACACCCATCCCGACGG
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GCAGAA

:::Rv159T7.seq:::

GGTATAGTCGCTGACCGGTGCAGGTTTCGACAATGTGGTGCCGGTTCGGCGGCTACGTGCCATCGAGACACTGGCGCA
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CGACACCCACGACGGAAAGACGCAGATCGCCGTCAAGCATGTGTGCCGCGGATTATCAGGACTGACCTCCTGGCTGAC
CGGCATGTTTGGTGCAGATGCCTGGCGCCCGGCCGGCTGGTCTGTTGCGCTCGGATAGCGAGGTGAGCGAATTCTC
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CTGGCGGCGGCCCA

Clone Rv15

:::Rv15SP6D2.seq:::

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CCCTNTCTAGA

:::Rv15T7.seq:::

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Clone Rv160

:::Rv160SP6.seq:::

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AGCGGGGCACTGCNATGTATGACACCGACGGCCGCCGATGGGCCAGGGTCTGGCAAATTCGATCTGTGCGGCCAGT
GCCAGCAGCGTCGCCTCGTCATACGGCCGCCGACGAGTTGAACCGACATGGGCAGGCCGTCGCCGTCGAAGTCCCAC
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:::Rv160T7.seq:::

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ATGGTTGCGGCACGGGTGTGAAATCACGGTGGCGGTAGCCGTTGCGCTGATTGGACCGCTCATCGCTGCGTTTCGCG
TAGCCCGCCCGCACAGGGCGTCGGCTTCAGCCCCCATCAAGCGCGGATGAACGTCGAGAGCAGCCCGCGCAGCAGA
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CCT

Clone Rv161

:::Rv161SP6.seq:::

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AATCGAGTTCAGGTCCAGCGGGTGGCGCAGCAACGGCGCGAGCTCAACNACGTCAATCACGTTGTGCTTTCTACGG
TCACCGACCCGGTGACCGTAGTCGCCCGGTGCGCTCGGCCGAGAAGTTGCACCGCCACCACCGCGACAACGCTTTGCA
CGCGGACGCCACCCCCCGAT

:::Rv161T7.seq:::

GCGCNAACAGCTCGCGGCAGCCACGACGTGCTGCGTCGGATTGCCGGCGGCGAGATCAATTCAGGCAGCTCCCGGA
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CAAGGAGGTTGTTGTGGTGCTATCGACGGCCTTTAGCCAGATGTTGGAATCGACTATCCGATAGTGTCCGCGCCAAT
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Clone Rv162

:::Rv162SP6.seq:::

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TCCACGCGGTGCGGCACATGGTGGACACCACCCGACCGCACGGGGTGAAGGCCTATGTCACCGGTCCGGCAGCAC
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TGTTGCTAGTGATCTATCGCTCCG

:::Rv162T7.seq:::

CCATGAGCACCGCCAGCCGAGCACGAGGCCAAACTCCGCCGACGCAGGCCGGTTGGACTTGTGCTGCTGGACAAGGGG
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GAAGCGAGGAGCATGGCCGCCGACCCGCAATGTACACGCTGCAAGCAAACCATCGAACCCGGATGGCTATACATCA
CCGCCCATCGCCGCGGTCAAGCCGGGATCGTCGATGACGGCGCAGTACTGATTACGTCGCCGGTGAATGCCGCACCC
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Clone Rv163

:::Rv163SP6.seq:::

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CGGACAGGTTGGGGTGCCTTTGGGGCAATNACAGGTGGCGGCGGTGCGTTCGGGTGCGCCGGCGGAGGTGCTGCNTTG
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CCT

:::Rv163T7.seq:::

CCAAGATCTACACCATCGAATACGACGGCGTCGCCGACTTTCGCCGGTACCCGCTCAACTTTGTGTCGACCCTCAACG
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CCAATACGGTCGGTCCCACGATGACCCAGTACTACATCATTTCGCACGGAGAACCTGCCGCTGCTAGAGCCACTGCGAT
CGGTGCCGATCGTGGGGANACCCACTGGCGAACCTGGGTTCAACCAAACCTTGAAGGTGATTGTTAACCTGGGCTACGG
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Clone Rv164

:::Rv164SP6.seq:::

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ACCTGGCGATCACCTGCCTCTCGTTGACGATCGATCGTCTATGCCGCCGTCTCTGCGGGAACAGGCCNCCAGTACATC
GCCACAGACGGGATCCACCCGCATTTTCGGCTACGGTTGCTCGTTTCGGTGTTTCGGACTAGTCGGTCCTGGTGACGTGC
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:::Rv164T7.seq:::

CGGGGGGCTCTTAATAGTGTAGGAAAGAAGCTCTACATATTTCAGGAGGATTACCATGGCTCGTGCGGTCGGGATCG
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GGACCACCCCGTCAATTGTGCGCTTCGCCCGCAACGGTGAGGTGCTGGTCTGCCAGCCCGCCAAGAACCAGGCAGTGA
CCAACGTCGATCGCACCGTGCGCTCGGTCAAGCGACACATGGGCAGCGACTGGTCCATAGAGATTGACGGCAAGAAAT
ACACCGCGCCGGAGATCAGCGCCCGCATTTCTGATGAAGCTGAAGCGCGACGCCGAGGCCTACCTCGGTGAGGACATTA
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Clone Rv165

:::Rv165SP6.seq:::

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ACAGCCACCACCCGAGTGGCGACCGAGTGTCCACCACGGACCGCAGCGATGCCGTACCTCACCCGTCCAGCGGTCC
ACCACGACACGGTCTGTGACCAGCGCGCGGGCATTCACCACCCAGGCGGTACCGCCAGGCCGATCGCCACACCCGCC
ACCATCCCCGATGCAGCCAGGCCGGGAGTAAGA

:::Rv165T7.seq:::

CTGGTGCTGGACGGAGCCTAGTACAACCTCCTCTCCAATGCTCTTGCCCCGATCGCGGCGACAGGATGACCCAGGAC
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TGTGCCGACAACCCATCGGTGTACGTCTGTCAGTGGTGGTTAGGTGCAGCGAGTTGCGCTGTTTGGCAACGACGGCGCC
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GCTGGATTCAAGTTGTAGAATAAAT

Clone Rv166

:::Rv166SP6.seq:::

ATACTCAAGCTTTTCCGGCGTCGTCCACCTGACCCAAAAGCGCAGGTGCGCCGCCAAACGGCCCGCTGGCCGCGCA
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:::Rv166T7.seq:::

TTTCAGATCTCATTTTTATGACATGACTGGAGATCTGTCTAGATTGCAGCTCCTGTGAGCGTGGGTACCGGATTCAAG
CCGGTCGGTCACGCCGCGGTGGTACCGGCTTTGCGGCAGTGCTCGGCCCTCAGTTTCGGCGATCGCGCGCAAGTGCGT
TTCGCGCACCAAGATCGCGGCCTAATGGCCGGCGATGACCGCGATGACCAGCGCGATCCAGGAAAAACCGTTCCAACC
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Clone Rv167

:::Rv167SP6.seq:::

ATACTCAAGCTTCCCGACCACAAGTTGAACAGCACCGATTTCGGCGAGCACTTCGTCAACTTCAGGGTGCCCGCACC
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TCCCGCGCTACCGGCTGCCTTGGCCCCGACGGGACCACGGTTTTTTGAGCTGGACCGCCCGAGGTCCTTGATTTCAAG
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:::Rv167T7.seq:::

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Clone Rv169

:::Rv169SP6.seq:::

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:::Rv169T7.seq:::

GGGGCCACTCCGCACAATCTGTACCCGACCAAGATCTACACCATCGAATACGACGGCGTCGCCGACTTTCGCGGTAC
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AACCTGCCGCTGCTAGAGCCACTGCGATCGGTGCCGATCGTGGGGAACCCACTGGCGAACCTGGTTCAACCAAACCTG
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Clone Rv16

:::Rv16SP6.seq:::

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GCGATGCCAATTTCNACNCCGTNCTGGCCCCGGCGGGCGCTCCCCGGTTGTCAAACACCTGCCGTGTTTCGTTACN
CACTGCCCCAACATCNAGCCCGANCNATCCNAGGTCCGTCCAACGCCTCCGCGGCTCNCCAACCTNCTCCNCTGATCN
TCCGCACCAAACACATGCCCGACTCCNTGCNCCNATTGCTTGNATCCCT

:::Rv16T7.seq:::

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CGGGTGTCCACACCGGAGGACCCGCGTCCGCGCGGTTCCGGCAGACGTTGTGGGAGTTCCTGCCCCGAGTGTATC
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TATCTGCGCAACGACGTGCTCAACGCGTGGCTGATGTCGGTGGTGTGTGGGGTGGGCTGATCGCGGTCTTCGGCCCC
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Clone Rv170

:::Rv170SP6.seq:::

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:::Rv170T7.seq:::

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ATCGCAGCGGCGTGACCCAAACACATCGCCGGTCAAGCACTCCGAATGCACCCGGACAGCACGTGCTCACCGTCGGC
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Clone Rv171

:::Rv171SP6.seq:::

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TCCTTGGCGTCACTCTTGTGGCAGCCACCGAGCGGTTGGTCCAGGATCTGGATGGGCAAAGTTGTGCGGCCCGGCCG
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:::Rv171T7.seq:::

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ACGCCTCCGTTGATAAGGCTTTCGGTCTCTTCCCCGGTCATCCCAAGCACCTTGCGGCAAATTTGAACGCTTTCCTGT
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Clone Rv172

:::Rv172SP6.seq:::

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CCCTATCCAGCACGGGCCGCGCGCTCCGCNCCAGCCGGCGACGGCGTTCATCCCGGAGATCGCCTCGCTAGCGCTGC
GGTGCGCCGCGGTCAAGCATGGGCGCCGTGGGGCCGATGACCACCGGGGCGT

:::Rv172T7.seq:::

TTCGGCGGGTCTGTAGATTGCGGTGCGCCACCCACAGGCACTCATGAACCGCAGCCCACGATCGATCTCGGTGG

Clone Rv173

:::Rv173SP6.seq:::

GCGCACCATCGCCAGTAGGTGCCGTGGTTCGGGCGCGTCGAGCCACCCGAGCGGAAACGCGAGTCCGAACAGCAACAG
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:::Rv173T7.seq:::

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Clone Rv174

:::Rv174SP6.seq:::

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:::Rv174T7.seq:::

TTGTCCAGGCGGGGAATCGGGCAGGAGACGACACCTTCGTTTCGGTTCGATCGTCGCGAACGGGTAGTTGGCCGCGAC
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Clone Rv175

:::Rv175SP6.seq:::

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:::Rv175T7.seq:::

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AGCCGGTGTGATCGCGCTTTCGGCGTGTAGTGGGTGCGCGCCCGACCCGGCAAAGGCCGGCCCGACACAACCCCGGA
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Clone Rv176

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Clone Rv177

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Clone Rv178

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Clone Rv179

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CAGCGTCGCCCGGGTAGTCGCCGCCCGGGCGGCTACAGTCTGAAACGCGATGACCATCGATGTGTGGATGCATCATC
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Clone Rv17

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::::::::::Rv17T7.seq::::::::::

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Clone Rv180

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Clone Rv181

::::::::::Rv181SP6.seq::::::::::

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Clone Rv182

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CAGCGCGTGGGCCCGCGGGTCCCCATCACAACTGAACCCCCAACAGGGGACATGCTTAGCGGTAGGGCGCGCGCCA
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Clone Rv183

:::Rv183T7.seq:::

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CGTTGCTTGCATAGCCGGGAGGCCCGGATCCGCAATGACGGATTCCATGCCAACGCTCCGAGTTGCATGCGGATCGA
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Clone Rv184

:::Rv184SP6.seq:::

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CCAGTACTACATCATTCGCACGGAGAACCTGCCGCTGCTAAAGCCACTGCGATCGGTGCCGATCGTGGGGAACCCACT
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CGGACAGGTTGGGGTGCGTTTGGGGCAATGACAGGTGGCGGGCGGTGCGTTCCGGTCCGCCGGCGGAGGTGCTGCGTTG
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Clone Rv185

:::Rv185SP6.seq:::

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CACCGTCGGCGTTGGGCCGGCGATCTCGCCGCGGACAGCGCGACATGTTCCAGTCTCTGATAGTGTGGTGTAGC
CGATGGCGCGAAACTCCCCATGACGAGTCGGAATCCGCGCCTCGGCGACCCGCTCAATGTGCTTCTCGTGCTTGCGCC
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GGGCCCCGATCCGATGCCCCCTCCAGTTGCGTGAGCAAGCAGCGGAGTCGTGCGGGGATCGATGGCCACGGGGTGT
CAATGGCGGATGGTCCGCTGCCCGCCGACTGGCTCTTGCGGGAGAGCCGATCTAGCACCACCGATCCGCGCACGTGGA
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Clone Rv186

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GAACAGAACTGAGGTTTTGTAAACGCCACCTTTATGGGCAGCAACCCCGATCACCGGTGGAAATACGTCTTCAGCAC
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Clone Rv187

:::Rv187SP6.seq:::

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::::::::::Rv187T7.seq::::::::::
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CTTTCGAGGTCGAGGTCGATACCGATTTGCGCATCCGCGAGCCGCACCCTGGACGACAGAACCGTGCCCTACGANTGCT
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Clone Rv188

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Clone Rv189

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Clone Rv18

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Clone Rv190

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Clone Rv191

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Clone Rv192

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Clone Rv193

::::::::::Rv193SP6.seq::::::::::

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Clone Rv194

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Clone Rv195

:::Rv195SP6.seq:::

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GCGGATTATCAGGACTGACCTCCTGGCTGACCGGCATGTTTGGTCGCGATGCCTGGCGCCCGGCCGGCGTGGTTCGTGG
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:::Rv195T7.seq:::

TGATCGCGCATCACCTGCTTCATAAACTGGAAGCAGCGCAGCGCTTCCTTTTGGGCCGCAACATGAGCCAGCCTCTCG
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ACGAACGACGCCAGTCCGCTACGTAACCCCTCCGCGACTGTCCATGGACAACAGCGCGTTCTCCACCGACCGGGCCCG
GGTGTGGGGTGTTCGCGGACCGGCAGCCAGGTGGTCCACACTGCCGACGGGCGCCGCGAGCCGTTACCCGACCGAGGC
CGCCGAGCAAGTCCGCCCGATCGCATCTCCAACCGGTTGCGGTAATGCAGGTTAGCTGGCGTACTCCTCGTCGCGC
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Clone Rv196

:::Rv196SP6.seq:::

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TCGCACAGGTTGGCCCAACCGGCCGCTTGATGCCCGGTGCGCAAGCCCGGAGTTGCCAAACCCAGCGTGATCAGG
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:::Rv196T7.seq:::

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GCAGCAACGGCGCGAGCTCAACGACGTCAATCACGTTGTGCGTTTCTACGGTACCGACCCGGTGACCGTNGTCGCC
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Clone Rv19

:::Rv19SP6.seq:::

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:::Rv19T7.seq:::

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Clone Rv1

:::Rv1SP6D2.seq:::

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:::Rv1T7.seq:::

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Clone Rv201

:Rv201SP6.seq::

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CACGGTACGGAAATTCGTCCAGAAGGAAATCTTCCCAATGCACCGGCCCTCGAACGTGGCAACAGCTACCCGCAAGA
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:Rv201T7.seq::

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TCGCCGCGGACCAACGCGACATGTTCCACGTCTCGTAGATGCTGGTGTAGCCGATGGCGCGAACTCCCCANGACAA
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Clone Rv204

:Rv204SP6.seq::

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CCGGTCAAC

Clone Rv205

:Rv205SP6.seq::

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TTCATCCTGACGCCGGAACAAATTGACGCAGCGGTTCCGCTGACCAATACGGTCCGTCACGATGACCCAGTACTAC
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:Rv205T7.seq::

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Clone Rv207

:Rv207SP6.seq::

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Clone Rv209

:Rv209SP6.seq::

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AGGCCCGANTCNAGGCCGAAGCATATAGCGCGGCCGACCGCATTTCTGCTCTGACCGCAAGCGCGACCTCAGCCGCAGC
CGGTGGAGCTACTGCTGCGCGCCATCACGCC

:Rv209T7.seq::

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GGTGACCCCTCTATGACGCGGCGGTGGGACACTGTGATCTAAGACCGGTCTGGGTCTTCTCCGGGCAAGGGTCTCAGT
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Clone Rv20

.....Rv20SP6.seq:.....
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GACGGCGCGCTGGCCCGGCGGAACGTGGTCTCGACACCATGATCNAAAACCTCCCGGGGAGGCGGAGGCGTTGCGTG
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.....Rv20T7.seq:.....

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CAGCCATGCGGTGTTGCTGGGAACGAATTTCTTTGGAATCAATACGATCCCGATCGCGCTCAATGAGGCCGACTATGC
GCGGATGTGGATTGAGGCGGCCACCAGATGAGTATCTATGAGGGCACCTCCGATGCGGCGCTGGCGTNGCACCGBA
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Clone Rv214

.....Rv214SP6.seq:.....
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.....Rv214T7.seq:.....

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Clone Rv215

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.....Rv215T7.seq:.....

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TGGCTGTGTGCTGTGATGAGCCTGTCTAAGTGGTGCGTAACCGTTGACGAGCCGCGGCCCTCGCTGCAAACATTGAA
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Clone Rv217

.....Rv217SP6.seq:.....
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.....Rv217T7.seq:.....

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Clone Rv218

.....Rv218SP6.seq:.....
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TCCTGGTCGCGTTTATTACCTGACCATACCCGAGAGGTCTTCTCAACACTATCACCCGGAGCACTTCTAGAGTAAAC
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Clone Rv219

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.....Rv219T7.seq:.....
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CGGCCGTGATCGACATCGTCACCGCCGCACCACTGCCCGGTCTCGGGTTCACGCAGCCGTTGCCGCCCGCAGCGGACG
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Clone Rv21

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Clone Rv220

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.....Rv220T7.seq:.....
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Clone Rv221

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::::::::::Rv221T7.seq::::::::::

NCCTGGTTCATGAACTGGAAGCAGCGCAGCGCTTCCTTTTCGGCCGCAACATGAGCCAGCCTCTCGTCGGCGGTTCGGG
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AGTCCGCTACGTAAACCCCTCCGCGACTGTCCATGGACAACAGCGCGTTCTCCACCGACCGGGGCCGGGTGTTGGGGTG
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Clone Rv222

::::::::::Rv222SP6.seq::::::::::

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CCCACGCCGCGACGGGCCAACCTCAGCGACTCGATTACCCCGGACGAAGTACTCTACAGGTGGCCGAAGAGCTCTTT
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::::::::::Rv222T7.seq::::::::::

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Clone Rv223

::::::::::Rv223IS1081N1400.seq::::::::::

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::::::::::Rv223SP6.seq::::::::::

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::::::::::Rv223T7.seq::::::::::

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Clone Rv224

::::::::::Rv224SP6.seq::::::::::

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TCGGGTTACGCATCCGTTTGGCCGCCGCC

::::::::::Rv224T7.seq::::::::::
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Clone Rv225

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::::::::::Rv225T7.seq::::::::::
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Clone Rv226

::::::::::Rv226SP6.seq::::::::::
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Clone Rv227

::::::::::Rv227SP6.seq::::::::::
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GCGTCATGCGCTCGGTTCCGC

::::::::::Rv227T7.seq::::::::::
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ACTTGCCCGGAGCTGCCCGGGTTCCTGTCGCGCAGCTCGGCGGCCCGGTGAGAAAGAAATTGCGCCAGGTTCGCACAC
TCCGCGCGTAGGCCAGCTGCTCCAGGGTGTCCGCATAGAGCCCGCGGGCCGACGCTGCTCGCTGTGCGCGAACACC
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Clone Rv228

::::::::::Rv228SP6.seq::::::::::
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CCCATCGAGTTCGAGTCGCTGGCGGCCACTTATGGCCTGGGTAAAGGCCAGGGCGAGAGCCCGTGCATTCGGGGTTCG
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GGGCACATTCCCCGCAACTTCACTTCACCCGGTGGAACCCGGCCATCAACACGTGCGCGACGCGGCTGTTTCGTGCCG
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::::::::::Rv228T7.seq::::::::::
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CGGTCTCTCGAGTATCTCCCGCACCGCCCCACCGGTGCGGTCTGCCCCGATCCACTTTGCCCTTGGGACGCGACC
AGTCGTGCTAACGGGGGCGGTGAATGACAGCGATCTCGACCGGCCCTTCCGAATCGGCACTGCCGGGTGCCGAGAACA
CCGACCGGGCGGCGTACACAATCCGGCCCGCGAGCGCCGGCGGGCGGACGANTTCTGGATCGACACCTCAACTCCTG
CAGGTCAATTCCGGCAAGCTGCTCGCGGTGCTGGATGTGGT

Clone Rv229

:::Rv229SP6.seq:::

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GAGCTACATCGGCTCGGCCGCCAGTGTTCGGGCCCTCTTTCGAGGTCGAGGCTATACCGATTGCGCATCCGCAGC
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:::Rv229T7.seq:::

TCCGTACGGCCCGGGTACGCTTCGGTCGCAGTGTGCGAGTGATAGATGACGACCGGGACCTCGTCGGCATCTTCCATA
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TGCCGCTCGGGACGCTCAGAGCCCTCGGGTCCGGCCAGCACTCCGCAGGCTTCGTGCGGGTGGTCGCGACGCGCATGG
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Clone Rv22

:::Rv22SP6.seq:::

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:::Rv22T7.seq:::

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ACCGGCGCACGATCACGGTCCCGGTGATCGGGCCGCTGCGGGCCAAGGAGAACACCCGCCGGGTGCAACGCCACCTCG
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Clone Rv230

:::Rv230SP6.seq:::

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GGTCGACTTGATCAAGTCGGGTGGATACCGGGTTCGGCGCCGGTGAAATTGAAACGGTGCTGCTCGGGCATCCGGACGT
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:::Rv230T7.seq:::

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TGGGCCAGGGTCTGGCAGATTGATCTGTGCGGCCAGTGCCAGCAGCGTCGCCTCGTCATACGGCCGGCCGACGAGT
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Clone Rv231

:::Rv231SP6.seq:::

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CCGATCGCACAGGTTGGCCACAACCGGCCGCTTGATGCCCGGTGCGCAAGCCCGGCAGTTGCCAAACCCAGCGTGAT
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:::Rv231T7.seq:::

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Clone Rv232

:::Rv232SP6.seq:::

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:::Rv232T7.seq:::

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ACATCGCCGGTCAAGCACTCCGAATGCACCGGACCAGCACGTCGTCACCGTCGGCGTTGGGCCCCGGCGATCTCGCCGC
GGACCATGCGCGACATGTTCCACGTCCTCGTANATGCTGGTGTAGCCGATGGCGCGAACTCCCCATGACGAGTCGGA
ATCCGCGCCTCGGCGACCCGCTCAATGTGCT

Clone Rv233

:::Rv233SP6.seq:::

CGGCATCTGGCGGCTGAACCTGTTCTTGGGCAACATGCCGAGGATCGCCTCTTCCACCACGCGGTGGGGTGGCGTTG
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GTCGCCGCTGATGGCGACCTTGTGCGCGTTGATCACGATNACNAATCACCGCCANCGACATTGGGGGCGAACGTCGGC
TGTGCTTGGCGCGCAGCAGGCTGCCGCCGCGACGCAAGGCGCAACCACACGTCGCTGGCGTCGATGACGTACCA
CCATCGCGTGGTGTACCCGCCTTGGGC

:::Rv233T7.seq:::

GCGGCAAAAATTGAAGCACTCNTGGCCACTNCCGCCGGGAGGGACAATCTCGGGCGGCTAGGGCTTCTCGCGGGAAGG
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CCTGGCCGGGCGATGATCTGCAGCGTCGCCGCGGGTAGTCGCCCCGGGCGGCTACAGTCTGAAACGCGATGACCATC
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CTATCCCGGA

Clone Rv234

:::Rv234SP6.seq:::

CGCGTTGAAGTGAAGGGGTGCCGCCGGCTCGAGCAGGCAAGCCATTTGTTTCGATGCGGTTACCGAAGATCTCTTCGG
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CGGGGTATGCCCGCGAGCAGGATTGGCGAGCGGNCGGTTCAGCCGGGTGAACCTTCGTCAGAGCTGACGCTGCGGTTG
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:::Rv234T7.seq:::

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GATTCCGTACACCGCCACGCCGATCAGGCCCTGGGCCAGCTGATTGGAGCTGGCGTATATGGCGGCGATGGTGACGAT
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CCGGGGTCAACAGGTTGACCATCC

Clone Rv235

:::Rv235SP6.seq:::

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:::Rv235T7.seq:::

GCATGCGGGTGATGCCGTTCTCAGTGCGCAACAGCGTTTCGACGCGGCATACCCAGCCGCACATGCCGTGCACGCCGNN
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Clone Rv237

:::Rv237SP6.seq:::

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ANATCTTGATGTCCTGGTGAATCCACGGTGACTTTGGAGTGGAAGGCGGCCATACTGATCGCGCGCGCCACCACATGA
GCTAGCGGCAGGAAAACCAGCAGCCGCTCACCTTGCGCAGCAGCGTCGGGTGATATGCCTGGCGCCC

::::::::::Rv237T7.seq::::::::::
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TGGTGGCGCCCTAGGCGAGCGAACGCTCACAAACGGCGGTGACCGCTTCTGGTCGTGCACCATCGAGCCGTGCCCAGC
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Clone Rv23

::::::::::Rv23T7.seq::::::::::
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CCGCCGGGCTGTGCTACTACCGCGACGGCTCTGACAGCGTCGCTGGCATGGCGACACCATTGGTCGCGGCAGCACTG
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Clone Rv240

::::::::::Rv240SP6.seq::::::::::
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::::::::::Rv240T7.seq::::::::::
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Clone Rv241

::::::::::Rv241SP6.seq::::::::::
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AACATTGCGGGATGGCAGCAACCTGG

::::::::::Rv241T7.seq::::::::::
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Clone Rv243

::::::::::Rv243SP6.seq::::::::::
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CTCCCTTGA

::::::::::Rv243T7.seq::::::::::
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Clone Rv244

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CACCGGTGGGTGGGCTGGGCTATGGCCTGCCATATCGGCCTGGTGTCTACN

.....Rv244T7.seq:.....
CCGATATCCGAGCCGATAGCTGGCGGGCTCGGGTGGTNGCCAGCGGCGCTGCGACGAAAGTGTGACCGTCATGAAACA
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Clone Rv245

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.....Rv245T7.seq:.....
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TCGAGGATGAACTCGGCGTTGGAATTGTCCAGCCGGCCCAATTTCATCGAGCGCAGATTTCGTACACATGGCCGGCGGCG
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Clone Rv246

.....Rv246SP6.seq:.....
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.....Rv246T7.seq:.....
CGCTGAAAGCCACCATTCGCGGGTCGGGCGCCGGGCTCGGGCCGCCAGGCTGCTCCGCTCGGTGATGGCACGCCACCG
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TTTCGAGGTGCGAGGTGCA

Clone Rv247

.....Rv247SP6.seq:.....
TGTAATTTGGGATGGGCAAAAAGCAAANCACCGCTGGCCACAAACGCGGGGAGGGACAATCTCGGGCGGCTAGGGCT
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.....Rv247T7.seq:.....
CTTGGGCAACATGCTGAGGATCGCCTTTTACCACGCGGTGCGGGTGGCGTTGCATTAGCTCACCGATGGTGCGCTTG
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Clone Rv249

.....Rv249SP6.seq:.....
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Clone Rv24

.....Rv24SP6.seq:.....
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.....Rv24T7.seq:.....
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Clone Rv251

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.....Rv251T7.seq:.....
GGGTGTGCCTGCTGTGTATGCACGGCATACGGACATCCTTCCCCTGAAGACCCGCGGTGGAACAGCCACGTGTCCATC
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Clone Rv252

.....Rv252T7.seq:.....
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CCCTCGGGCCGCGCTGGCGGGCTGATGA

Clone Rv253

.....Rv253SP6.seq:.....
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.....Rv253T7.seq:.....
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Clone Rv254

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.....Rv254T7.seq:.....
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Clone Rv255

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.....Rv255T7.seq:.....

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Clone Rv257

.....Rv257SP6.seq:.....

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ATTCGTCAACAGATATCATCAATGTGGCGCTGGACTATTCAAATCATCGATATACTGGTGACCTGGTCTTCGCCAT
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.....Rv257T7.seq:.....

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TGTCACCGGACGGGTCGATCCCCAGTCCGACATTGAGGTGCTCGAGACCGAGCTGATCCTGGCAGATCTGAAACCCCT
GGAGCGGGCCACGGGCGGGCTGGAGAATGAAGCGCGCACCAACAAGGCGCGCAAGCCGGTCTACGAAGCGGCACTGCG
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Clone Rv258

.....Rv258SP6.seq:.....

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GGATCGTCCGGGCAACTCGCGCCCTCGGCCTGTGCGAACGGCACACCCGTGCTGGCGGCNCCCCGCGCGGAAGTGGGC
TCATCACGGTCTGTGCGAGCCGGTCCGCTACCGCGTACCGACGCCGTC

.....Rv258T7.seq:.....

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TGCCGAGTGTGTCGCCATCTCATGGCTCCAAATATGGAATTAGGTCCCTGGGCGGACTGACGACAGTCCCTCAGCGAC
CGGATTGCGCATCCCGCCTTGTACGCTACTCCGCAAATCCCGGGCTTGGCTCCGCGGAAGCGAACTCGGCGGCGCTAC
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ATTGAGT

Clone Rv259

.....Rv259SP6.seq:.....

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GCCGCCACCGGAATCGGCCAGCCGACCGAATGGGCCAGCGTTGCCAGCATCAGTCCGGCGCCGGCCGACACCAAGTGA
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TCGCCGGCGACGCTTGTTCCTCCATACTCGCCCCCTAATCTCGAGGACGCGGTACCCGCGAGGCAACCTCCCAAAAA
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Clone Rv25

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GAGGAATGTGCGACGTCTTGATGCAGCCTGTCAGAACACCGAGACCCTCGACGAACTTACGATCGAAACCGCTTAGGC
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Clone Rv260

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Clone Rv261

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Clone Rv262

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Clone Rv263

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Clone Rv264

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Clone Rv265

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Clone Rv266

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Clone Rv267

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Clone Rv268

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CAN

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Clone Rv269

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Clone Rv26

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Clone Rv270

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Clone Rv271

::::::::::Rv271SP6.seq::::::::::

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GAGCCGAGCGCCGTGAGATGTACGACCGGGTGGTCTATGTGCCGCGGTGGTGAGTTTCCACGACCTGACCATCGAAG
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::::::::::Rv271T7.seq::::::::::

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CTCAGGCCACCGAAATCATTCCCGGCTGGCTGCACGACTGCGACGTGGTCACCTCCAGGTGCAAGGGCTGGGCGA
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Clone Rv272

::::::::::Rv272SP6.seq::::::::::

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::::::::::Rv272T7.seq::::::::::

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Clone Rv273

::::::::::Rv273SP6.seq::::::::::

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::::::::::Rv273T7.seq::::::::::

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Clone Rv274

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::::::::::Rv274T7.seq::::::::::

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GAAGGTGGCGCCGGGGTGCCGGATCTGCCGTCGCTGGATCGTCTGGTGTGCGGCTGGCGATTGTGCCAGCAGCTGGC
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Clone Rv275

::::::::::Rv275SP6.seq::::::::::

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Clone Rv276

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Clone Rv277

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Clone Rv278

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Clone Rv279

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Clone Rv27

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Clone Rv280

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Clone Rv281

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:::Rv281T7.seq:::

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Clone Rv282

:::Rv282SP6.seq:::

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:::Rv282T7.seq:::

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Clone Rv283

:::Rv283SP6.seq:::

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:::Rv283T7.seq:::

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Clone Rv284

:::Rv284SP6.seq:::

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:::Rv284T7.seq:::

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Clone Rv285

:::Rv285SP6.seq:::

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::::::::::Rv285T7.seq::::::::::

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Clone Rv286

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GCTCAACCGCCCCGAACAGCTCAACACCATCGTCCCGCCCATGCCGACGAGATCGAGGCCGCTATCGGGTTGGCCGA
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::::::::::Rv286T7.seq::::::::::

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Clone Rv287

::::::::::Rv287SP6.seq::::::::::

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::::::::::Rv287T7.seq::::::::::

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CAATGCCGTGTCATAGATTCCCTCGCCGTCAGAGGGGTCCAGCAGGGGCCCCGAAAAGATACCAGGGGCGCCGTC
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Clone Rv288

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AGGTGCGCGATCGCGTCTCGGGCTTCGGGGAGCAGACTGACCTGCAGATGGAAGTCGTGCCACATGCCCGCGAACCGG
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GCGGTCTGCATGACGAATGGGCG

::::::::::Rv288T7.seq::::::::::

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CGTCACCTTTCCACGAGACCTCACCTGCCGATCCGAAATGGAATCGGCCGTCGACGGAATTGGCGCAGCGAACACTCAA
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GATCCGAAAGCTGCAAGCTCCCAGCACCGATCCCGACGTATCACCGCTGCCGCCCGGCACGTTCTTGAACCTATTTCG
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Clone Rv289

:::Rv289SP6.seq:::

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:::Rv289T7.seq:::

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Clone Rv28

:::Rv28SP6.seq:::

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:::Rv28T7.seq:::

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Clone Rv290

:::Rv290SP6.seq:::

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:::Rv290T7.seq:::

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Clone Rv291

:::Rv291SP6.seq:::

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:::Rv291T7.seq:::

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Clone Rv292

:::Rv292SP6.seq:::

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CCGGCGACGCTTGTTTCTCTCCATACTCGCCCCCTAATCTCGAGGCAGCCCGTACCCGCAGGCAACCTCCCCAAAATGC
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::::::::::Rv292T7.seq::::::::::

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ATGGGCCAGCGTTGCCATCATCAGTCCGGCGCCGGCCGACACCACTGACGGCAACGGTGAAATCNCGTGGGCGGCAAC
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Clone Rv293

::::::::::Rv293SP6.seq::::::::::

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::::::::::Rv293T7.seq::::::::::

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Clone Rv294

::::::::::Rv294SP6.seq::::::::::

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::::::::::Rv294T7.seq::::::::::

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Clone Rv295

::::::::::Rv295SP6.seq::::::::::

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::::::::::Rv295T7.seq::::::::::

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Clone Rv296

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Clone Rv29

.....Rv29SP6.seq:.....
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.....Rv29T7.seq:.....
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Clone Rv2

.....Rv2SP6.seq:.....
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Clone Rv301

.....Rv301SP6.seq:.....
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Clone Rv302

:::Rv302SP6.seq:::

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:::Rv302T7.seq:::

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Clone Rv303

:::Rv303SP6.seq:::

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GGATTATCAGGACTGACCTCCTGGCTGACCGGCTGTTTGGTCNCGATGCCTGGCGCCCGGCGGCGT

:::Rv303T7.seq:::

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Clone Rv304

:::Rv304SP6.seq:::

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CCCGGGGTGCTGGTGACCTGCCGATCGCACAGGTTGGCCCAACCGGCCGCTTGATGCCCGGTGCGCAAGCCCGGC
AGTTGCCAAACCCAGCGTGATCAGGCTCGGCTCGCGAGTTTCGGCGAAGAAGTGGCTCGCCTGATCACCTACCATCGGC
CAGGATCTGCGTGTATCACNACGCTCGCCAAGGAGGTTGTTGTGGTGTCT

:::Rv304T7.seq:::

GCCACGTTTCGCGCCGCCCGGCATACGGCGGCGTACCGATCTCCGCGTCATACACCCGCGGGTAATCGCCGACGGTGC
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Clone Rv306

:::Rv306SP6.seq:::

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:::Rv306T7.seq:::

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Clone Rv307

:::Rv307SP6.seq:::

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:::Rv307T7.seq:::

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CCACCGTCGTGAAGACCCAGATTGAAGGTGTTTCGTGCTCTACGACATGACCCCGGCGGACGAGAAGAACCCTTG
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Clone Rv308

:::Rv308SP6.seq:::

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:::Rv308T7.seq:::

CGNCCAACCCGAATTGGTTTTTCGGCGCCNTCGGTGAGGACGGCGTGCGGGTGCTCAACGACGACGTCGTCCGCGGGAC
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Clone Rv309

:::Rv309SP6.seq:::

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CATCCTGACGCGCGGAACAAATTGACNCAGCGGTTCCNCTGACCAATACGGTCGGTCCCACGATGACCCANTACTACNT
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:::Rv309T7.seq:::

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TGGGCGCGTTGGTGACCGGCAATACCTACCGCAGCCCCAGCCCTGCTGGCAAAGATCATCACCACGCTCGACGTGGTTA
GCGCCGGTCGAGCGATCCTCGGCATTGGAGCCGTTGGTTTGAAGTGAACACCGCCAGCTCGGCTTCGAGTTCGGCA
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Clone Rv30

:::Rv30SP6.seq:::

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GCCCCGACGGTCCCCGCCGATGCCGTGCTGTGCCCCATGTTGCTCTTGGCCGATCCAAGCGCGCAGGGGGTGCCCCGCGC
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CCGTTTCGGGCTG

:::Rv30T7PEG.seq:::

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CCGTGATNTCACCGCCGACGTAGTTGGCGTTGTGGTCCGCCATCCGCGCGGCGGGCACGGCGCGGGCCGCCACCACGA
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GGGCATATGTCCANAACGGACGNGGCCGGTTTCNTCGATGCNGCCGGGGTCCGCGACNTGCGGACNCNCNGNCACACC
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Clone Rv310

.....Rv310SP6.seq:.....
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CGCGTCAACAACCTCCCGGGTGAAGTGAATANCACTTGCCGA

.....Rv310T7.seq:.....
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Clone Rv311

.....Rv311SP6.seq:.....
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.....Rv311T7.seq:.....
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Clone Rv312

.....Rv312SP6.seq:.....
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Clone Rv313

.....Rv313SP6.seq:.....
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ACGCAATTATTGATGTGGTAGGCGGCAGCTGCCGTTTTGTGCTGTCGG

.....Rv313T7.seq:.....
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CGCAGCATGCACAAACGCGTACACCGCTGTCACCAAGACGGCGACCAGCAATACCAGCATGACGGTACCCACGAGGTG
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Clone Rv314

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Clone Rv315

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.....Rv315T7.seq:.....
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Clone Rv316

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.....Rv316T7.seq:.....
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GGGCGCGTTGGTGACCGGAATACCTACCGCAGCCCGACCTGCTGGCAAAGATCATCACCACGCTCGACGTGGTTAG
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Clone Rv317

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::::::::::Rv317T7.seq::::::::::

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TGTCGACGTTTCCGTGCGATCAGCGTGCAGCGGCGACCCACTCNACGAGGTCTCGGTGCCGCCGCGGCCAGGGCACCA
GCAGTGACGAGTCCAGGCGCCGTCGGGCCAAGCAGTCCGCGTGCCANCCGTGGTGGGTCGGGCGATGGTTGGGTGTGC
TCATTTCCGGGAACGCCA

Clone Rv318

::::::::::Rv318SP6.seq::::::::::

CTCGAAGCTTTAACAGCATCAACCCGCCCCGACCCAGCACCAGACACNATGTCGATGCCATCGAGGTGAATGTCGAAC
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CCGCTCTACCGCAGGTGACCTCGATCACCAGAGACCANCCGGCCGTTNTNNTCAGCACCCCTACCGTGTACGCCCA
AAACGGCGCTGGTGGTCGATTGCCGGAGTGCACCCNCACCCAGTGTCTGTGCECGGATCC

::::::::::Rv318T7.seq::::::::::

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CCGTGGAAGACNAACGTGTCCGGTGTGCAGGCCGCGGAGAAGGCGCGGGCGACNTCTTGGGTTTCGTCTANAGATAC
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Clone Rv319

::::::::::Rv319SP6.seq::::::::::

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ACGCTGAAGTTGGTGTCTCCATGGACTTGGGGATGTGCCTGAACCGGTTACCTACNACTCCAAGCTGGCGCCGTCT
CGTCCGCGAGGTGCTTGGCTTGCATAGCCGGGAGGCCCGGATCCGCAATGACGGATTCCNTGCCANCGCTCCGAGTTGC
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::::::::::Rv319T7.seq::::::::::

GTTTTGGCTCGGCATGGTTAGCCAAGGTTCTGCGGTCCCACAGATCATCTTGGTCCGGTAGCGCTCGTCCGGGTATG
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TCACAACTGAACCCCCAACAGGGACATGCTTAGCGGTAGGGCGCGCGCCAAGGCGGCAGCAATCGCATCACTGCGCT
GCGCGTCACTATTAAACCCACCCGACTTCACTTCCAGACCCCGAATGGCGCCCGGTCACTGATCATCTGCGCACCG
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Clone Rv31

::::::::::Rv31SP6.seq::::::::::

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GTCGACTGGTTCAACCATCGCCGCTTACCGGTACTGCGGCGACATCCGCGGCTTAACCTCGACGCCGCTCACTA
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::::::::::Rv31T7.seq::::::::::

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TCTGGGTCA

Clone Rv321

::::::::::Rv321SP6.seq::::::::::

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AAAAAGTATGAGAAAATCCATGCAGGCTGAAGGAAACAGCAATAACTGTGACAAATTACCCTCAGTAGGTGAGAACA

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Clone Rv322

:::Rv322SP6.seq:::

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GATGCCGGGATTTCCAGCCGCACTAGGATGTCTAGCCGGCCAGCCGCTGCCGCCGGACTTCGGGATGTTCCGGTATACC
ANCGATCGGCAATCTTGCGTATCCGCCGATGCTCGAACGCTANCCACGCCAAACCAACCACTGTGACNACAATCGCCA
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:::Rv322T7.seq:::

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CCGGACCCATCAACATCTCGATCATCGACATTCGGGCGCTGCCGGGCTTTGGCAACTCGACCGAGCTGCCGTCGTCCG
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Clone Rv327

:::Rv327SP6.seq:::

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:::Rv327T7.seq:::

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AACCTATTGCTGTGAGCTTCATTTGCTGCGAGCAAAACAGTTGGTCGGCCGTTAGGAACTGAATTGACACTCAACCGA
TTTGGTGCCNCCGTAGGTGTCTGGCTGCGGGTGCGCTGGTGTGTCGCGGTGTGGTAACGACCACAATGTGACCGGG
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Clone Rv328

:::Rv328SP6.seq:::

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CGTGGCCATCACGTCCGGGTGTCCACACCGGAGGACCCGGCGTCGGCGCGGTTTCGGCGAAACGTTGTGGGAGTTCCTG
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CT

:::Rv328T7.seq:::

GCACCAAGGCCCCACACGTCAACCCTGTGACCTCCTGCGCCGACCCCGCCCGAGGTCCTGGCCGTTACCACCTGAACGG
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GGGTCNATCCATTTCAGGTCCGTGCGCGCGTCGGTCGAGTGGCGGTACACTCCAGGTACTCGACCTCACAGACGAGA
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Clone Rv329

:::Rv329SP6.seq:::

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GCCGCGATCTCCAGGCTCCGCCGAGCCAGGTGCATCCCGGTCCGGATCCCACTAACCCGGCACCATTTGGCGTCN

:::Rv329T7.seq:::

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GGATTTCGACGCCCTTGTAACCCAACTTCGGCAAGTCCCGCGACACCGTGAGTCCCGGCCCGGGTTCGACGAGCAGCAT
CGACATGCCTTGGTGCCGCGGTGTGGCGTTCGGGTCGG

Clone Rv32

:::Rv32SP6.seq:::

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TGGCCGCGTGTCCGCANGTCCCNAAACCCGGCCGCACCGACGAAACCCGGCCGCCGTCCGTCTGGACCAACGCTCATGT
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:::Rv32T7.seq:::

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GGCGCCACCGCGAGGTAACCTCGTCTCAGTCCCATACGCGACCGGGTATCCACGTGCGCGCAACAACGCCACCACCTC
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Clone Rv330

:::Rv330SP6.seq:::

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TGCCGGAATGGGGATGTCCGGCACGGCGAAACCGTAGTTCTGCTTGTCCCGTGAGGCCAGGTGGATGGGGGGAAAGAT
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:::Rv330T7.seq:::

CGGCGACGTGCGGATACGCCGAGCAGTTGGGAATCGCTCTGCAGCAAACCAATATTCTGCGCGACGTTTCGAGAGGACT
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CACTCGATGACCCCGACGGACGGCTCGCGGCNCTGCTGCGGTTCAGTGCCGACCGCGCCGAGACTGGTNTTCGCTGG
GACTGCGGCTGATTCCACACCTCGACCGCCGCGAGCGCTGCCTGCTGTGCGGCCATGTCTGGCATCTACCGCCGTGAGC
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Clone Rv331

:::Rv331SP6.seq:::

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CCGGGCGGAGCTACATCGGCTCGGCCGCCAGTGTTCCGGCCCTCTTTCGAGGTCNAGGTCNATACCGATTTCGCGCAT
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:::Rv331T7.seq:::

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Clone Rv333

:::Rv333SP6.seq:::

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CGGGGTCNATCCATTTCGAGGTCCGTGCGCCGCTCGGTTCNAGTGGCGGTACACTCCAGGTACTCGACCTCACAGACNA
AAGGACTCNATCCCATAGGTGTGGACNAAACAGATCTTCTGTCCGACNACTACACCACCACCCAGGCCATCGCCGC
CGCCGCGATGCCAACTTCGACGCCGTACTGGCCCCGGCGGGGGCGCTCCCGGTTGTCAACACTTGCCGTGTTCTNT
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Clone Rv334

:::Rv334T7.seq:::

GTTCTTGGGCCCATGCGGAGGTATCGCCGTTTCCACCACGCGGTGCGGGTGGCGTTGCATTAGCTCACCGATGGTGCG
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Clone Rv335

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CACCGBAATTATCCGTGCCATGGCTGGTACCGGGGGAGTGGTGACGGCTGCCGGCATGGTGTTCGCCGTTACCATGTC
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Clone Rv336

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Clone Rv337

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GGTGCGGCACATGGTGGACACCACACCGCCACCGCACGGGGTGAAGGCCTATGTCACCGGTCCGGCANCACTCAATGC
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Clone Rv338

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Clone Rv339

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TAGCGCCACGATCGTCNAAATNTCCGCTGAATCATCGGATAGCTGATCCGGCGTCAACGCGTTTTGANTTCACCGC
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TGGGTAAGCGTC

Clone Rv33

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CACCATCTGTACCCGACCAAGATCTAC

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GCAGTGACGGCCGGCCCGAACATTACGCGCTCGTTGATTAGGCGTTCCGTCTCGTCCGCGGTCTATGCCGAGCAGCTTG
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Clone Rv340

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Clone Rv341

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Clone Rv343

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Clone Rv344

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CGGCCGGCCCGAACATTACNCGCTCGTTGATTAGGCGTTCCGGTCTCGTCCGCGGTTCATGCCGAGCAGCTTGCGGCANA
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Clone Rv346

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ACCACGGCGGGCGTCCGGCGTCGTCACTGCTCGANATCTCAGCATCCGCAGCCGGTGTGATCGCGCTTTCGGCGTG
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CGCGCAGCAGACCGGTGGGTGGGCTACGGCTGCTATTTCGGCCTGGTGTCTACGTCTCGTTGTTGCCGTGG
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Clone Rv347

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ACCACTTTGGAATTGGACCTTGATGTACGGCCCATCGACGGCGACGGCACCTGCAGGTACTCCACCGGCAAGCCCCG
CCGGGAAAATGCCCCCGCGGTCTCCGTGCCACCGACGGCGCCGANCAAACCCGACACTAGGGCCGCGCCNACGGCCCC
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CGGGCCGAGGCCGGTGCATACCGTATTGCGTCAATTGGGACGCGGTTGTGCATTCCGGCTAGCTCGGTTGCCACACCC
GTCAGGGGTTGACGTTGGCGGGTTCGGCGGGCCCCANACCGCTGTCAACATGCCCGCCAAGCCGACCTGCGGCGCC
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Clone Rv348

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GCCGACGGCGACGCGGTAGGTGGTCAAGTCCGGTCTACGCTTGGGCCTTTGCGGACGGTCCCGACGCTGGTTCGCGGT
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.....Rv348T7.seq:.....

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CTTGATCATCACTCTGCACACGACCTGCGAACCCCGCGCGGCTTGGCGACCTGGAGCAGCTGGCGCAACGTGTGAG
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Clone Rv349

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TGGTCNACTTCTTCTCTCACGG

::::::::::Rv349T7.seq::::::::::

TCGACGGTTTGGCGGCCTTAAATGCACTGAGGTCGTCAATTGACCCACAGCGGAAATGCCGACTATTGCGAGGCCTC
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GTGCCTTGTNTANGATNANCTCGGCGTTGGAATTGTCCAGCCGGCCCAATTCATCGAGCGCANATTTCGTACACNTGGC
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Clone Rv34

::::::::::Rv34SP6.seq::::::::::

GACCACGCCAGGCTAATCACGTGACGCTACCGAATACCCTNCCTAGTGGTGCAGGCTCCCGCTGGAAATGGCCCTGTA
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::::::::::Rv34T7.seq::::::::::

CGGCACCCGACCCCTTTGAGCCGTCCGCCGTGGCCGGTGGAATGGCCGACGAGGGACTGATCGTGCTGGGCAAAT
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Clone Rv350

::::::::::Rv350SP6.seq::::::::::

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CGCTGTGCGACCGACGGNGCANNACCGTGAGGCTAGGGAAGCGAGGAGCACATGGCCGCCGACCCGCAATGTACACGCT
GCAAGCAAACCATCGAACCCGGATGGCTATNCNTCACCGCCCATCGCCGCGGT

::::::::::Rv350T7.seq::::::::::

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ACCACACCGCCACCGCACGGGTGAAGGCCCTATGTACCGGTCCGGCAGCACTCAATGCCGACCAGGCCGAGGCCGGA
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Clone Rv351

::::::::::Rv351SP6.seq::::::::::

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::::::::::Rv351T7.seq::::::::::

TGTCAAGTCCTTTCAGATCTCNTTTTATGACATGACTGGAGATCTGTCTAGATTGCAGCTCCTGTGAGCGTGGGTAC
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Clone Rv352

::::::::::Rv352SP6.seq::::::::::

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::::::::::Rv352T7.seq::::::::::

TACGCTGGCGCTGGAGGGAGCCANNTACAACATCCACGCCAATGCTCTTGCCCCGATCGCGGCGACCAGGATGACCCA
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GGAGTGTGCCGACAACGCATCGGTGTACGTCGTCGGTGGTGGCAAGGTGCAGCGAGTTGCGCTGTTTGGCAACGACGG
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Clone Rv353

:::Rv353SP6.seq:::

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GACCGANCGGCTGCNNNTGGGCGCGTTGGTGACCGGCAATACCTACCGCAGCCCGACCCTGCTGGCAAANATCATCAC
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:::Rv353T7.seq:::

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GGTCCACGATGACCCAGTACTACATCATTCGCACGGAGAACCTGCCGCTGCTAGAGCCACTGCGATCGGTGCCGATC
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Clone Rv354

:::Rv354SP6.seq:::

CTCAAGCTTGCCGGGAGGGTGCATGGCCGACTCGGATTTACCCACCANGGGGCGCCAACGCGGTGTCCGCGCCGTCNA
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GGATTTGACGCGCGTGCCGACCTGAGGTTGGCGGTGGACGAGGTGTGACCCCGGTTGATTGCTCGCGCCTTGCCGGA
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:::Rv354T7.seq:::

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TGTAAGCCCGGCCAGCGCGCCGACGGAGATGATGCCGCTGGCCAGTACACCCGTTGGCCTGGAACGCGGTGGCCA
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Clone Rv355

:::Rv355SP6.seq:::

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:::Rv355T7.seq:::

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GATTTTGGCGGCTACCCGCGATTACCCGCGCGGCTCGACGAGTTTTTGGCCTGGACTACCCGCGTGCCCAATCTGCT
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Clone Rv356

:::Rv356SP6.seq:::

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:::Rv356T7.seq:::

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CGCCGCGATCGCC

Clone Rv357

:::Rv357SP6.seq:::

TACTCATGANCATCCTTTAATCANNGCTTTGCGTTTTTTTATTAAATCTTGCAATTTACTGCAAAGCAACAACAAAT
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CAGTCACTTATTATCACTAGCGCTCGCCGCAGCCGTGTAACCGAGCATAGCGAGCGAACTGGCGAGGAAGCAAAGAAG
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Clone Rv358

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.....Rv358T7.seq:.....

CATGGTGGCACTGTAGCGACGTGCTGCAATCAAGGTCAATGCCCGACTCTGGTCAGCTCGGANCCGCTGACACCCCGCT
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GTTGCGGGCGAACTTCATCATCAGCTTGGACGGCGGCGCTACCGTCGATGGCACCAGCGGGGCGATGGCCGGGCCCCG
CGACCGATTCTGTTCAACCTGTTGCGTGAACCTGCCGACGTCATCGTGGTCGGCGTGGGCACCGTGGCATTGAGGG
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Clone Rv359

.....Rv359SP6.seq:.....
TACTCAAGCTTGCGGGTGATCGCCTTGGTCAACGGCACCGTGATCGGATCGGGGTCNACCGCACAAATGGACTGGAGC
TTCGGCGAANTCATCGCCTATGCCTCGCGGGGGGTGACGCTGACCCCGGTGACNTGTTTCGGCTCGGGCACGGTGCCC
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.....Rv359T7.seq:.....

GTTGGNGCCTCGTCGGCGAACAGTTCTCGCACGATTTCCGGATTAGCGGGACTGGTCACCAGTTGGGTATGCGGGAAG
GCGCTGACGTTCCGCGCGATTAGCTGTTTGATGGACGCGGTGGTGATGTTCTGATCACGGAAGTGGCTGTAATAGCCC
AGGGTCGCCACGCTTTTCATCCGGGCCCCGACCCGGCGCACCGAGCGTGTCGCGCAGGTATGCGACGTGATTTTCGCTG
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Clone Rv35

.....Rv35SP6.seq:.....
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CCACCGCCGCCGGAGACGCTGCCTTTGTACCGAATACAACAACGCCGCCGAGGCGTTTCGCAGCCCAGCTGGTGACCG
CCGAGCAGAGCGTCGAAGACCTCAAGACGCTGCATGACCAGGCGCTTAGCGCCGCAGCTCAGGCCAAGAATGCCGTCG
AACGAAATGCGATGGTGCTGCGGCATAAGATCGCCGAGCGAACCAAGCTGCTCAGCCAGCTCGAGCAGGCGAAGATGC
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.....Rv35T7.seq:.....

CAGGCATGCAAGCTTCGGAGGCAGACCCGTGCATGGTGGCACTGTAGCGACGTGCTGCAATCAAGGTCAATGCCCGACT
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AGCTTTACGACTATCCGGATGACGGCACCTGGTTGCGGGCGAACTTCATCAGCAGCTTGGACGGCGGCGCTACCGTCG
ATGGCACCAGCGGGGCGATGGCCGGGCCCCGCGACCGATTCTGTTCAACCTGTTGCGTGAACCTGCCGACGTCATCG
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Clone Rv360

.....Rv360SP6.seq:.....
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ACCGTGGCGGTACAGTCCGGGTGTCCACACCGAGGACCCGGCGTCCGGCGGTTCCGGCNAAAGTTGTGGGANTTCC
TGCCCCGCANTGTTATCGGCGGCTTGCCT

.....Rv360T7.seq:.....

GGCCATCGCCACCGCNCCGCGGCGAACGCTCAAAGGCACCTACTGGCACCAAGGCCCCACACGTCACCCTGTGACCTC
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GCAAGGTGCATGGGCGGAGTTGTTCCGCCACTTCGTGATGACGGGGTCGATCCATTCCAGGTCCGTGCGCCGCTCGG
TCGAGTGGCGGTACACTCCANGTACTCGACCTCACAGACGAGAGGACTCGATCCCATCTAGGTGTGGACGAAACAGA
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Clone Rv361

.....Rv361SP6.seq:.....
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CGCTCGTCAAGCACCTCNGGCCACCGGAATCATTCCCGGGCTGGCTGCACNACGGCGACNTGGTCNCCCTCCAGGTGCG
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.....Rv361T7.seq:.....

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GGCCCGGACCCGGCGCACCGAGCGTGTGCGCGAGGTATGCGACGTGATTTTCGCTGAAGTCCCGTACCCGGAGAACT
CGAACACGCTGAGGCGCTCGTCACCGTGTNNCGGCGACCAAGCGCGGCGAGCAACTGCGCAAAATCGTTAAGANAGG
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Clone Rv363

.....Rv363SP6.seq:.....

CACAAGACAATACTCAAGCTTCAGGTCAATGTGCNCCAAGCCCTGACGCTGGCCGACCAAGGCCACCGCCGCGGANAC
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AACCTCAAGACGCTGCATGACCAGGCGCTTANCGCCNACGCTCAGGCCAAGAAGGCGCTCGAACGAAATGCGATGGTG
CTGCAGCANANATCGCCGANCGAACCAAGCTGCTCAGCCAGCTCGAGCAG

.....Rv363T7.seq:.....

CCACCCGTGCATGGTGGCACTGTAGCGACGTGCTGCAATCAAGGTGATGCCCGACTCTGGTCAGCTCGGAGCCGCTGA
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CGGCACCTGCTTGC GG GCGAACTTCATCAGCAGCTTGACGCGGCGGCTACCGTCGATGGCACCAGCGGGCGATGGC
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Clone Rv364

.....Rv364SP6.seq:.....

GCTTTCCGCCGATACCCNCCATGTCCCGCACATCCAGGACTTCTGGGGGGATCCGCTGACAGCGGCGGGATCCCAAAG
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GGTG

.....Rv364T7.seq:.....

CAACCCGANTTGGCTTTCGGCGCCNTCGGTGAGGACGGCGTGCGGGTGCTCAACGACGACGTCGTCCGCGGGACACAC
CTCGATGCTGCCGCATGGACGCGGTGCAACGCAAGCAGCTGATCGATCTACNACGCCGNGNGGAACGTTTCNGCCGC
GGGCGTGACCGCNTCCCGTT

Clone Rv365

.....Rv365SP6.seq:.....

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TAGCACCTGGCCGGGCGATGATCTGCCAGCGTCCCCGCGGGTAGTCGCCGCCCGGGCGG

.....Rv365T7.seq:.....

CAGCAGACCAACAAGAGCATCGGGACATACGGAGTCAACTACCCGGCCAACGGTGATTTCTTGCCCGCCGCTGACGGC
GCGAACGACGCCAGCGACCATTTCAGCAGATGGCCAGCGCGTGCCGGGGCCACGAGGTTGGTGCTCGGCGGCTACTCC
CACGGTT

Clone Rv366

.....Rv366SP6.seq:.....

CTCAAGCTTGACTGGCCACCCACCGCATGACCACCGACAGGCCCGACTGGTCGTACCACTCGAACGCCGGGGTGTTT
GA

.....Rv366T7.seq:.....

TTGGTGCCCGGAATGGCGAGTCCCATTTANTCGCTGATTTGTTTGAACAGCGACGAAACCGGTGTTGAAAATGTCGCC
TGGGTGCGGGATTCCCTCTCCAAGCAAGAGTAACTGGCCCCAAATAAAGTTACTCGTCGTCTTGCAAAGACCGCTACC

CGATGCCATTTATGTGTTTCCTTACGCTCNNNNNTCCGGTGCGCCATCATTATCTGCACCTTTGCACTGCACATTGAG
CTTAGCAGCGCTCG

Clone Rv367

.....Rv367T7.seq:.....
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TGACCGCATCCCGTTGACCGGGCGGATCGCNGTGATCGTCGATGACGGCATCGCCACCGGAGCGACGGCCAAGGCGGC
GTGCCAGGTGCGCCGGGCGCACGGTGCGGACAAGGTGGTGCTGGCGGTCCCGATCGGCCAGACGACATCGTGCGGAG
ATTCGCCGGGTACGCCGATGAAGTGGTGT

Clone Rv368

.....Rv368SP6.seq:.....
TAAAGCTTTTCGTACGTTTATNGNGCCCCCGACCAACAAAAGCATCGGGACATACGGAGTCAACTACCCGGCCAACGG
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GAGGTTGGTGCTCGGCGGCTACTCCAGGGTGCGGGCGTGATCNACATCGTCACCGCCGACCACTGCCCGGCCCTCGG
GTTACGCGAGCCGTTGCCGCCCGCAGCGGACGATCACNTCGCCGCGATCGCCCTGTTGCGGAATCCCTCGGGCCGCGC
TGCGGGGCTGATGAGCGCCCTGACCCCTCAATTGCGGTCCAANACCATCNACCTCTGCAACAACGGCGACCCGATTTG
TTCGGACGGCAACCGGTGGCGANCGCACCT

.....Rv368T7.seq:.....
CCGGGAGGGACCATCNCGGCGGCTNCGGCTTCTCTCCGGAAGGTTCTANNGTNNNGCGTTTCNACNCTTCCCGTCGC
CCTGCGACCGCCGAACATTCGGGGTATGGNNGCANCTGTNAGCATCCNGGCCGGGC

Clone Rv369

.....Rv369SP6.seq:.....
CTCAAGCTTCCGCATCAGATCGCTATAGAACC GGTCGCGTCCCCACCGAGTGGCTGGTCGCCTTCCAGCACGATCGT
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GCTCATCGATACCGAGTGTGCTTTCCGACCACTTCCAGTTGCGGTACGGCGAGATTGACAAAGGCGGTGAAGCCCAG
CCAGAGCAGGACGATCACCNCCGCAAACCGGCGGATTGCCCCG

.....Rv369T7.seq:.....
GCTTGGCAGCCTGCGGCTGGGCGCCCTNGAGCTCTTCGATCTGGATCTCCGGACTCGAGATGCTCACTTGCCCGGCCG
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GGTCGACGCCGGTAACGGTCAGCAGCTCCGANGTCCNNCTGATCCCGACCGCAGCTGCCAATGCGCGGCTGGCAGCCG
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GCCTGCCGCAN

Clone Rv36

.....Rv36SP6.seq:.....
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.....Rv36T7.seq:.....
CAGGCATGCAAGCTTGTGCTCTATCACATCCGACCACCAACCGCCCCGACGGCTCGGCAGAACGCCTCCGCATATGGGT
CGACGACCGAGCGGGTCGGACTTCTGGGCTGCCAGCGCTCGCGCCGTGCGGACAAACAGCGCGGTGGAACCGACACTCC
TTGTGATGTCCACCTATCACCTTCGGTACGCACCCAATCGACCCTACGCGGCTAGCTCAGCCCCGATCTTCCAGAGC
TCCGCCCC

Clone Rv370

.....Rv370SP6.seq:.....
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AGTCGCTGCGGTGCAGCCACCTCATTTGGCGATGGCGCCGACNATGGCGCCTGGACCGATCTTGTGCCGCTTGCCGA
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.....Rv370T7.seq:.....
CGANCCTGTTTCGACGGCTACCTGAATCACCCCGATNCCACCGCCGCGGCGTTTCGACGCCGACAGCTGGTACCGCACCG
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Clone Rv371

.....Rv371SP6.seq:.....
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.....Rv371T7.seq:.....
CGCTGGNCGCCGCGCTGGGCTGCGGTAACCAATTACCACAACACTTTTCGGTAGCCGAACAGCGGCGCGTACCAGCG
AAATGGCACAGCCACCGCAGTCGCGGACATCCCGCGAAGATGTGGCAGATTTTCGTGCGGTCGAGCCGGCGAAGGCCT
AGCGTCATTGTTGCCTGGCAAGGTTGCTGGGCCCGG

Clone Rv373

.....Rv373SP6.seq:.....
CTCAAGCTTCTTCTGCCCCCTTGCCGTTNCGGATNACATCCCGCAGCGACTCGGCTTCGGCGTCGATGTGCAAGTTCTC
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GTTTTCTGTCNACNATCAGCTGCTTGCGGCCANCTTGGTGAAAGTGCTCCAAATGTCCTCCAACCGGTCCAGCTCAGC
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.....Rv373T7.seq:.....
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TCGGGATGCAAAGCCGGGCGAGCAATTCNCCNACACCATCTTGCCGTAAGAACCTGGAGATCGAACCCCGCGGTT
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Clone Rv374

.....Rv374SP6.seq:.....
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.....Rv374T7.seq:.....
TCCNCATGGGATAACGGGTTTAGATTTNACAACGGCACCGTGTTTCTCAACAAGCCGGTCATCAGCTGGGCGGGCG
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TGGTCCGCAAGTACGCGTTCTACTACCGCTATGACACCGCCGAGGAACGCGCCGTGCTCAACCGGATGTGGAAGCTGG
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Clone Rv375

.....Rv375SP6.seq:.....
CTCAAGCTTGGGTGTTGCCGATCACCGGAAGCCNATGATCAGCCACGTTTCGCGCCGCCCGGCATACGGCGGCGTAC
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CNAGTTCCANGTCCAGCGGGT

.....Rv375T7.seq:.....
TNAACAGCTCGCGGCAGCCACGACCTGCTGCGTCGATTGCCGGCGGCGAGATCAATTCCAGGCAGCTCCCGGACAA
TGCGGCTCTGCTGGCCCGCAACGAANGACTCGAGGTACCCCGGTGCCCGGGTTCGTGGTGCACCTGCCGATCGCACA
GGTTGGCCCAACCGGCGCTTGATGNNNNGTGCGCAAGCCCGGCAGTNGCCAAACCCAGCGTGATCANGCTCGGCT
CGCGAGTTCGGCGAANAAGTGGCTCGCCTGATCACCTACCATCGGCCANGATCTGCGTGTCA

Clone Rv376

.....Rv376SP6.seq.....
GCCANCCGGCTTGGCGTCGACTCCCGTTCNGCACATCATACGGTCCCCGGTACTGTCCAAGTGCGCCGGTGGCGTAGC
CAAACGTCACGACTCTCAGTGATCCCAGTTCGTGATCCGGCCGGTGGCGCCGCTGCGGCGGGGGCTNATNTACTTCGG
ACTNATTATCTCATCCAAAGGACACCGGGCCGGTGGCTGGAATCCCATGGTGCGATCGGCCACACAN

.....Rv376T7.seq.....
CCGACCTGGTATCTTCCGATAGCGCGCTTGATATCCGGTCTGATCTCCTGCCCTTAACGCCGGATCTCAGCAGGTCC
CCATGCAAAGATCCGAGGTGTCCNGATCTAGGGGTCTCGTCTCCAGATGATGGAGCAAGTCGGCCC

Clone Rv377

.....Rv377SP6.seq.....
CTCAAGCTTCGCTCAGGCGGCGCTGCCGGTAACGTCGCTGACCGGTGCAGGTTTCGACAATGTGGTGCCGGTTCGGC
GGCTACGTGCCATCAAGACACTGGCGCAGGCTATCGCACCCGTTATCGGCTACAAACAAATCGCGGTATGC

.....Rv377T7.seq.....
CATCACCTGNTTCATGAAGTGAAGCACCGCAGCGCTTCCTTTTCGGCCGCAACATGAGCCAGCCTCTCGTCGGCGGT
CGGGTGCAGGTGCTCGGGCAGCTCGGCCGCGACAGCCGCTGACCCGTAAACAGCTTCCATATCCCGCGACGAACGA
CGCCAGTCCGCTACGTAACCCCTCCGCGACTGTCCATGGACAACAGCGGTTCTCCACCGACCGGGCCCGGGTGTGGG
GTGT

Clone Rv378

.....Rv378SP6.seq.....
AGCTTAGCTTCCCGCCCCGGCAATAGGGCTCCAGCTCATCCGGTGTGACCAGATAGGGGCCAGGGTGATACCGCTGT
CTTTGCCCTTGGCCTGTCCGATGCGCAGCTGGCCCTCCAGCATCTGCAGGTCCCGTGCGGACCAAGTCGTTGAAATGG
TATAGCCGATGATCGACCG

.....Rv378T7.seq.....
CCNGAACAGAAGCGNGGTTCTACCGCGGTGTGCGGCCGGCGCGATATCGGCCTTTTTACTAACCGAACCCGATGTG
GGCTCCGATCCGGCGCGCATGGCATCGACGGCGACGCCGATCGATGACCGCCAGGCTTACCACCTT

Clone Rv379

.....Rv379SP6.seq.....
CTCAAGCTTGCAGGACTCGACAAGCATTTCTTGACAGTTGTTTTGGCTCGGCATGGTTAGCCAAGGTTCTGCGGTCCCA
CCAGATCATCTTGGTCCGGTAGCGCTCGTCCGGGTATGCTGCCGCCGGGATTCTCGCTGCTATTACTCCCCCGAAGA
ACGCCACCGGTCCAGCGC

.....Rv379T7.seq.....
GCNAGGCGGTATAGCTTCCCGTCTACCGGCGACCGCCAGCCGAGAAGCTCGTTTTCCAGTGTTGCTGGGGATTCTC
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AAGTTGGTGTTCTCCATGGACTTGGGGATGT

Clone Rv37

.....Rv37SP6.seq.....
GTGTGGAACCGTGAGCGGATAACAATTTACACAGGAAACAGCTNTGACCTTGATTACGCCAAGCTATTTAGGTGAGG
CTATATTAATACTCAAGATTGCGGTCGAGCACATCGGCCCAAGAACCGCCGAAGGCACGGCGGAACGCCTGCGGCACA
TGGGGCGACGACACGCGGTTCGACTTCTGGGCTGTCCAGCCGGATCGCGCCGTCGCGA

.....Rv37T7.seq.....
CACTGTCAGTACATATGCGCCGCTCCTCCTCATCGCTCGGCTCGGCATCGTCGCCGGCGGTTCATGGCGTCACCCCTACC
CAAGCCGAACGCGAAGACGAGAACGTGTTCCATTATTAGGGTGTGAGCACCAATACCAGATTGCTCACCAGGAACCTCAC
GCAGCACCGGGACGGATGTCAGCCACCACGCCCATCTGGGGTGGTAGCGGGGAAATACGGCTAACGCGGCTCCGGTGC
CGGCAGCCAGCGCAGACCTCGGCGGCGGACACGGCAAACAACGACGACCCATAGTTGTTCTTTGCCGGATGGCCGT
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CCAGCCAAACCGTGA

Clone Rv381

.....Rv381SP6.seq:.....
CTCAAGCTTTTACGGTGATCGCGCATCACCTGGTTCATGAACTGGAAGCAGCGCAGCGCTTCCTTTTCGGCCGCAACA
TGAGCCANCCTCTCGTCGGCGGTTCGGGTGCAGGTGCTCGGGCAGCTCGGCCGCGACAGCCGCCTGACCCTGAAACCAG
CTTCCATATCCCGCGACNAACGAC

.....Rv381T7.seq:.....
CTCAGAAGCCGCTAGCTGGTAGAGTCGCTGACCGGTGCACGTGGCGNCAATGTGCGCTGCCGGTTCGCG

Clone Rv382

.....Rv382SP6.seq:.....
CTCAAGCTTTCGCTCATCAAGCGCGAACAGCGGGCGGTTCGGCTGGTCGCCATGACGGGTGACGGGACCAATGACGCA
CCCGCGCTCGCGCAAGCCGATGTCGGGGTGGCNATNAATACCGGCACCCAGGCGGCCCGGGAAGCCGGCAACATGGTC
NATCTCCACTCC

.....Rv382T7.seq:.....
ACTTCTATTTGCACTGGTGTGCTGTGGCGCGATCCGACTGCCGGCGTGGTCAAGGCCGGCCAGTTGTGGGATNCCACA
GGCAC

Clone Rv383

.....Rv383SP6.seq:.....
GCTTGTTCGTATTCCGTGGCACTGTCAGACATATGCGCCGCTCCTCCTCATCGCTGCGCTCGGCATCGTCGCCGGCGGT
CATGGCGTCACCCTACCCAAGCCGAACGCGAAACGAGAACGTGTTCCATTATTAGGGTGTGAGCACCAATACCAGATT
GCTCACCAGGAACCTAC

.....Rv383T7.seq:.....
CGATATTCGTCGGCCGCGTTGTCTCGACTGGGTTCGCGT

Clone Rv384

.....Rv384SP6.seq:.....
GACCTCGGCCACCAAGCCGGACGCGACCGTCGAGGTGGCGATCCGGCTTGGCGTCGACCCGCGTAAGGCAGACCACAT
GGTCCGCGGCACGGCCANCCTGCCACACGGCACTGGTAAGACTGCCCGCGTCGCGGCN

.....Rv384T7.seq:.....
CCGGAAGTCTAGGGGACGACCTACTCAGCGCAAAATGTCGCTAATGTGAGTCCGCCCCACCAGGGCAGATCAACCCAT
GTCGATGATGACCTACCCGGATACCCGATTGGCGGT

Clone Rv385

.....Rv385SP6.seq:.....
AGCTTCAGTTCCTCCACGACGCGTTCCTCAATGAATTTCCCGATCCCAATCTCGGTTTCAGATACAGGTTCGCCATAC
CCCTTACTTCGGNAACGCTGGGCGGATTGGCCCTGCCGCTG

.....Rv385T7.seq:.....
CCGCTACGGGTGCAACATGCATCCCGAGACCGATGCTCGAGCGCGCACCCCACTCGCCGATGGCCGGAACCGGTGG
TTACCCGGGTGGCGGCTGACC

Clone Rv386

.....Rv386SP6.seq:.....
GCGGCTGGTTACGACTCCCTGTTTGTGATGGACCACTTCTACCAACTGCCCATGTTGGGGACGCCCCGACCAGCCGATG
CTGGAGGCCCTACACGGCCCTTGGTGGCTGGCCACGGCGACCGAGCGGCTGCAACTGGGCGCNTTGGTNACCGGCAAT
ACCTACCGCAGCCCGACCTGCTGGCAAAGATCATCACCACGCTCGACGTGGTTAGCGCCGCTCGAGCGATCCTCGGC
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.....Rv386T7.seq:.....
GCCTTTCGCACAATCTGTACCCAGGACCNTCTAAAAATCGAATACGACGGCGTCGCCGACTTTCCGCGGTACCCG
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CAAATTGACGCAGCGGTTCCGCTGACCANTNNTGTGGTCCCACGATGACCCAGTACTACATCATTCGCACGGAGAAC

CTGCCGCTGCTAGAGCCACTGCGATCGGTGCCGATCGTGGGGAACCCACTGGCGAACCTGGTTCAACCAAACCTTGAAG
GTGATTGTAACTGG

Clone Rv387

:Rv387T7.seq:::

GCAGACCAACAAGATGCATCGGGATCATACGCCGTCAACTACCCGGCCAACGGTGATTTCTTGGCCGCCGCCAC

Clone Rv388

:Rv388SP6.seq:::

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CGTAAGGCANACCANATGGTTGCGGACCGGTCAACCTGCCACACGGCACTGGTAANACTGCCCGCGTCGCGGTATTC
GCGGTTGGTGAAAAGGCCGATGCTGCCGTTGCCGCGGGGGCGGATGTTGTCGGGAGTGACAATCTGATCGANAGGATT
CAGGGCGGCTGGCTGGAATTCGATGCCGCGATCGCGACACCGGATCAGATGGCCAAAGTCGGTCNCATCGCTCGGGTG
CTGGGTC

:Rv388T7.seq:::

CCACGGCGTGGATCAAGGTACCGGCCGGGATGTTGCGCAATGGCAGGTTGTTGCCCGGCTTGATGTCGGCGTTAGCGC
CGGATTCACCACATCCCCTTGCGAAAGTCCGTTGGGTGCAATGATGTAGCGCTTCTCCCATCGAGATAGTGGAGCA
ACGCAATCCGTGCGGTACGGTTCCGGGTCNTACTCGATGTGCGCGACCTTGGCGTTGACACCATCTTTGTCATTGCGGC
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Clone Rv389

:Rv389SP6.seq:::

GGCGGCTGCGTCGCGGAGATGATCGCCCGGTGCCACCCCGATCCGTGCCTCGGTGAGCGCCAACGTGCTTCCGGTCC
GGCGACCACCATGTCGATGCGCCGAC

:Rv389T7.seq:::

GCAATCGCCTTGGCGGTGCGCGGTTGTACCGGTGATCATCNCGGNGCGGATGCTCATNCGGCGCATTTTCGTCNAAT
CGTTCCCGTATGCCACCTTGACGATGTCCTTCATATGGACCACGCCGATGGCCCNCGCGCTNCTG

Clone Rv38

:Rv38SP6.seq:::

CCGGCTCGTATGTTGTGTGGAATTGTGAGCGGATAACAATTCACACAGGAAACAGCTATGACCATGATTACGCCAAG
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GGCATCGCCAAGGTGGACTTCTTGCTCAGCGACGAGATCCCGTGGTCGGATCCGCGGCTGCGGCGGGCTGCGACCCCTG
CATCTCGGCGGACCCGTGACCAAGATGGCGCGCGCCGAGGCAGACGTGCGCGGCGGGACGCCACGCCGACTGGCCGATG
GTGCTGGCCGCGTGTCCGCACGTGCGCCGACCCCGGCCGATCGACGAAACCGGCCGCGCTCCGTTCTGGACCTATGCC
CACGTGCCGTGCGGGTCCACGCTCGACGCGACCGAGACCGT

:Rv38T7.seq:::

CGCGTCCACCGCAGCGTGAGATTGGTGGCGCCATTTCGTGCTGTTGGCGGCGTCGCCGTATTGTGCG
GGCCAGCCTTGTGCGGGGCGGCTTCTACCCACGAGTCGGCACTTCCGCAACCGCCAGCTCGACCGCGATTACGGCG
GCCGCAACGGCGCGGGAAGCGTCTCGCAAGCGCCTTATCCTTTCGAGGTTCCAGATCCTTCCGCTACGTGGGTC
GCTCATCGGCGGGCCCGGCGAATGAGTACAGGTGAGGGTAACCGCTACAAATGAAGTTGGTCAGTGCTGGCCAACTG
TGTAATGGTTGCCCGGCTCGGGTCACCACGTACATTCTGGCAAGGCGGGCGAGATTGCGTTCTCGCGTCTTGGCCG
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Clone Rv390

:Rv390SP6.seq:::

CTCAAGCTTGCGCTGGATCTGGCGGCTGAGCCTGTTCTTGGGCAACATGCCGAGGGATCGCCTTTTCCACCACGCGGT
CGGGGTGGCGTTGCATTAGCTCACCAGTGGTGCGCTTGTGCAGGCCGCCGGGATACCCGAGTGCCGGTAAACCATCT
TGTGCTGCAGTTTGTGCGCGTGTGCGGACCTTGTGCGCGTTGATCACNATGACNAAGTCACCGCCATCGACATTGG
GGGCGAACGTCGGCTTGTGCTTGCCGCGCAGCAGGTTGGCCGCCGCGACGGCAAGGCGGCCAANCACCACGTC

.....Rv390T7.seq:.....

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GCGGGAAGGCCCGAACGTACGGCGTTTCAACACGTCGCGTCGCCCTCCGACCGCGAACATTTCGGGGATGGCAGCAACC
TGGTAGCACCTTGGCCGGGCGATGATCTGCAGCGTCGCCGCGGGTAGTCGCCGCCCGGGCGGCTACAGTCTGAAACGC
GATGACCATCGATGTGTGGATGCAGCATCCGACGCAACGGTTCCTACACGGCGATATGTTTCGCTCGCTGCGCCGGTG
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Clone Rv391

.....Rv391SP6.seq:.....

CTCAAGCTTCGTCATAAGACCATGGTGCCTTTCTTTACCCGTCANAGTCGGGGGCATCCGCACCGGCTCGCATCG
CATCATCCTCCACGACGGGCCGCTCATCAGCTTGGGCCATTTCAATGTACTTGATAACCCGCGCTGCGGGTAGGCCA
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.....Rv391T7.seq:.....

GAATTCTGCGTGACCGCTATGGGTTCAGCAGCGGCTGGCGCCGCACACCCACTGGCCCGGGTGTTCGCCCCGA
ACCCGGATCATGGTGAGCGAAAAGGAGATTGCGCTGTTGATGCTGGGATTTCGCCACCGCGAGGCCATCGACCGATTA
CTCGCCACCGGGGTGCGAGAGGTGCCGCACTCCCGCTCCGTCGACGTCTCCGACGATCCATCCGGCTTCCGCCGTCGG
GTGGCGGTAGCCGTCGATGAAATCGCTGCCGGCCGCTACCACAAGGTGATTCTGTCCCGTTGTGTGCAAGTGCCTTTC
GCGATCGACTTTCCGTTGACCTACCGGCTGGGGCGCTCTGCACAACACCCCGGTGAGGTGCTTTTGTTCAGTTGGGC
GGAATCCGTGCTCTGGGTTACAGCCCCGAACTCGTNCGGCGGTGCGCGC

Clone Rv392

.....Rv392SP6.seq:.....

GCAGTTGGGAATCGCTCTGCAGCAAACANTATTCTGCGCGACGTTTCGAGAGGACTNNTTGAATGGACGGATCTACCT
GCCGCGCGACGAGCTGGACCGATTAGGCGTACNCTCCGCCTGGACGACTCCGGGGCACTCGATGACCCCGACGGACG
GCTCGCGGCACTGCTGCGGTTTCANTGCCNACC CGCGCCGANACTGGTATTTCGCTGGGACTGCGGCTGATTCCACACCT
CGACCGCCGCGACGCTGCGCTGCTGTGCGGCCATGTCTGGCATCTACCGCCGTCNGCTCGCCTTGATCAGACCATCGCC
GGCGGTGCTCTACCATCGGCGAATCTCTGTTTCGGGACTGAANAANGCCCAAGTGGCGGGCGGACGACTGGNCTCTT
CGGTAACCTGCNGACCGCCCATTTGACCGCTACCG

.....Rv392T7.seq:.....

TTGATCTGGACGTCTGAGACGGTGATCGNCCGAACCTGAATTGTCCGGTAATGCCAGCGCAGAAAGCANGGTGGTG
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AAGCCGTAGTTTCGCTTGTCCCGTGAGGCCANGTGGATGGGGGAAGGATCGTGGTGTCCGGGATGATAATGGGGCCG
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CCGGTGTGGC

Clone Rv393

.....Rv393SP6.seq:.....

CACGTAGGCGCCGTCATAAATNACTCCGCCGCGCTTCGCACATCCTCGTANCGATCCTTGCGGAGCAGGTCAACCGG
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GAGGACNAGGTACGAANCTGCGCCAGCCGGTCGTACCGCTCAGGGCGGATGTGCGCGGTCCGCCACCCGCGTACCGC
CCGATCGGACACCTGTATGACCGCGGCGACNTCGACCTGGGTGACGCCGAAGGGTTTCAGGGCATCNACNATCTCGCT
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.....Rv393T7.seq:.....

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TGACATTGCCGGCCAGCGTCGACCTGGAAAAAGAAACGGTGATCACC GGCCGCTAGTGGACGGTGACGGCCAGGCCG
TGGCGGCGCGTTTCGTGCGGCTGCTGGGACNCCTCCGACGAGTTACCGCCGGGAGGTGCTGCGCTCGGCCACCGGG
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Clone Rv396

.....Rv396SP6.seq:.....

CTCAAGCTTTGTCCGACAAGCGTTCGCCGGCGGTGACGAAGCGAACGTGCGTTGGCCCACTGCGGGTCGATATTGCCG
CCAGGGA

.....Rv396T7.seq:.....

CGTCAGCACGGCGACGTCGCGNTACGCCGAGCAGTTACACAATCGCTCTGCAGCAAACCAATATTCTGCGCGACGTTTC
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Clone Rv39

.....Rv39SP6.seq:.....
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TGGCCAATCTGGCATCGTCGATCANCATGTGGTGGGGGGTGACCTCGGCGGTGATCGAAATACCCTGGTCCCTTATCCC
ATTTAGGATTTTCGACGGTGCCCGCGGCCGACGCGTGACAGATGTGCACCCGGGCGCCGGCGTCACGGGCCAGCAAGG
CGTCGCGGGCGACGATCGATTCTCGGCGGCCCGCGGCCATCCCCGCCAGGCCCGCCGCGCCGATGGGTCCCTCGT
GCGCGACGGCGCCGACCGTCAGCCGGGGCTCCTCGGCGTGCTGGGCGATCAGCACGCCCAAACCGGTG

.....Rv39T7.seq:.....
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Clone Rv3

.....Rv3SP6.seq:.....
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GGGCGCAACCGCGGTGTCGCGCCGTCGAGCTGAACGTTGCTGCCCGCTGGAGAACCCTGGCGCTGCTGCGCACCCCTG
GTCGGCGCCATCGGCACCTTCGAGGACCTGGATTTTCGACGCCGTGGCCGACCTGAGGTTGGCGGTGGACGANGTGTGC
ACCCGGTTGATTCGCTCGGCCTTGCCGGATGCCACCCTGCGCCTGGTGGTTCGATCCGCGAAAAGACGAAGTTGTGGTG
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.....Rv3T7.seq:.....
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ACCACCGTGGTAAGCCCGGCCAGCGCGCCGACGGAGATGATGCCGCTGGCCAGTACACCCGTTGGCCTGGAACCGG
GTGGCCAGATTTGCCGGCCCGCGGCCCGGTACGGTCCGCGAGTTGGGTGTATGGAACCATGCCCGACAGCACCCGAT
ACCGCGACGTAGAGAAGGGTCACGACCCCGACGACGCGAGAATCCCTCGAGGGACGTCTCGTTGAGGACGCTTGGTC
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Clone Rv40

.....Rv40SP6.seq:.....
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CGCCAAGCTATTTAGGTGACACTATAGAATACTCAAGCTTGCTCCTCGGGCGTGGCCTCGGCCAAGAAATCGTCGACGC
CGGCCTCCTGTGCAATCGCCTTGGCGGTGCGCGGGTTGTACCGGTGATCATCACGGTGCGGATGCTCATTGCGCGCA
TTTCGTGCAAGCGTTCCCGTATGCCCACCTTGACGATGTCTTCAGATGGACGACGCCGATGGCCCGCGCGCTGCTGT
TATCGGTCCATTCCGCAACGACTAGGGGTGTCCCCCGCGGAGTGATGCCGTGACAAATGGCACCCACCTCCTCAG
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.....Rv40T7.seq:.....
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CGGCCTGCCCTGGGTATCCCGCGCGCATGACGAGCAGCAGCAATTCGCCGAGCTGCTGGCTTCCCGCGGTGCGGAAGT
GCTGTTGCTGTGCGACCTGTTGACTGAGGCACTACATCACAGCGGGCCGCCGCGATGCAGGGGATCGCCGCTGCCGT
CGACGACCGCGGCTGGGACTGCCGCTGGCGCAAGAACTTTCGGCCTACCTGCGTATCTCGACCCAAGCANGTTGGCG
CATGTGCTGACGCCGGCATGACTTCAACGAAGTCCCNCTCCGACACGCCGAACGAAGTGTGCTTGGTGTGCGTATGC

Clone Rv412

.....Rv412SP6.seq:.....
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GTGCTGATGATCTCCCGTGAATGTGCCCTCGCCGCCGTCTATCGAAAACAGTGAGCATGCTGCG

.....Rv412T7.seq:.....
CAACCGCGCTCGGGCGCTCTGGGCTTCCGCCGGCTCCGCCGACAATTCTATCTCTGGATCAGCGGGGCTCTCCGGGC
CGGCCTCCGCGAATCAACAGGCCGCGCTTCCGGCCGAAACATTCCCTAGCCATATATGATCGCACCTCGATACACG
ATCTGGCGGCAACACCGCAAAGCGTCCGACGGGCCAACCTCCGCAATTCAGGTATCCGGG

Clone Rv413

.....Rv413SP6.seq:.....
GAAGGTCGGCGAAGGTGTGGCTGGNTGCCGATCACGAATCCAATGATGCAGTGGTCGGAAGATATTAGCCACTTGCTG
TTCTGGAGACAGGTGCTGATGATCTCCCGTGAATGTCCCTCGACTCCGTCTATCGAAATCTGTGAACA

.....Rv413T7.seq:.....
TCCTGCGCTCTGGGCCATTCTCGGGTCTGCCGACAATTCTATCTCTGGATCTGTGGGGCTCTCTTGGCCGGCCTCNGC
GATCTCTTCANGGCGCGCTTCCGGCCGAAACATTCCCTATCCATATATGATCGCACCTCTATACACCGTTTGGCGGC
AACACCGCAAAGTGTCTGTCG

Clone Rv414

.....Rv414SP6.seq:.....
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GGGCTTGCGCGCCAAACTGGCCACCGCAACAACTTGGCTGAGCTTGATC

.....Rv414T7.seq:.....
CTCTATCTGGCGTCACATTCGCAATCTTTAGATTGCAGATATCGATAAAATCACCCGCGCGACAAGACCGCCATGTCA
TCCTTTTCGATGTTATTTCCGCCGCTGGGGAAAGCGCAACGACGTTGCCTACACGTTCCGCCGT

Clone Rv415

.....Rv415SP6.seq:.....
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CGATCAGCGAGCCCTCCCTGCTGATTCCCTTGCCGTAGAGGATGTGCAACTCGGCCTGCTTGAAGGGGGCGAACAGT
TGTGCACGACAACCCCTTCGGCGACGAGGGTGTGCAGTTCTCGACCTCGAGGTGCAACGTTCTGCCCCGCCGCGTTG
GCAGCACTTCTCGGATCACGGAATAGCGGANTTCTTCCGCCAGCATGTCGTGCAGGAATTTGTCATCCAGGGCATCCG
CGAGCGCCTGCACGCG

.....Rv415T7.seq:.....
ACTGTCNAGGGAATGCTTCGCAGCATCTACCTGCAGTCGCTTGTGCATAAGCGGACGGCCCNACCTGTTCTGTTCCG
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ACCCGTCCGCAAGACGCGGTCAACGACCTGTTTCAGGCGATCAGGGTCACCGACTCACCTGCACTGAGAACAAGCGAT
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Clone Rv416

.....Rv416SP6.seq:.....
TGAATTATGATCCCGACACAATTCANTTTAGCCGCGTCGNGATGCTATCCGCCGACGGTTTGGANCNGGTCCGT
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CGCCAACAAGGCGGCAGCGGCTGCGACCACGCAGGTGCTGGCCGCGGGCGCCGATNAGGTGTCAGCGCGCATCGCGGC
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.....Rv416T7.seq:.....
AACGGGGACCNCAAGAAACCATTCANAACGAGGGGTGCTCACCAACGTCGAAACCGACGGTTGCCAGCCGGCCACG
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TTAGCAGCCGAGCTCAAGGTGTCCCGACCACTGTCTCGAATGCTTTTAACCGACCGGATCAGCTCTCCGCCGATCTA
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AAAGCCGGTGCGGT

Clone Rv417

.....Rv417SP6.seq:.....
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AAGGTCGGCATGGAGATGGAGCTGACGACCATGCCGCTGTTGCCGACNACGACGGTGTGCAGCGCATCGTCTACGCG
TGGCGGATCCCATCGCGCGCCGCGACNATGCANAGCGCANCGATCGTGAGGAGCGGCGCCGATGAGGATGAGCGCGC
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.....Rv417T7.seq:.....
TTCTCNCATCGTTCTGACTNNGATGGGACGCTGCTGCCCGAGGCGATCCTGGCCAACCGGCTCTCGCCGGCGCTGACC
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ACGAAAGATATTCCCGTCTACCGCTTCGTATTACGTGCTTACGCCGCGCAGCTGGTGCAAACCATGTCAACCTCACC
TGGTCGATCGAAGGGGGTTCGGACCAAGCAACGGGCAAGCTACGGCCACCGGTGTTTCGGGATCCTGCGTTACATCACCGAT
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Clone Rv418

.....Rv418SP6.seq:.....
TTCTTCCGGGTACCGCTGATCGGCGGCACCATCACGCACCCGGTGCAGGGCGAGGCGGCCCGGTTGGTGTTGCTA
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ATCTTGGCCAAGTCGCTGGGCAGTGACAACGCGATCAATGTGGTGACGCCACCGTGGCCGCGCTCAAGCTGCTGCAC
CGTCCGGAGGAGGTGGCGGCGCGCCGCGGTTTGCCAATAGAAGACGTCCCCCGGCCGGGATGCTG

.....Rv418T7.seq:.....
GTCGAAAGTGACCATCTCTACCTTGAGTGCCATACCGCCGACCCTATGCCTCGGATAGCTCGGCGGAAAGAAACGCT
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CCGACGTGACCGTGGGGATTCCGGTGCGCGCCGCGGCCAACGGCCCGATCGTCGACCCGACGGCAGATCGGCGCGA
TGTTTCGTAACGCTGCATAGGCACTCCCGCGCGCTGGCAGGCCAGTTGCGAAACGCCCCCGCGGGTGCCTTCCGTGCG
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Clone Rv419

.....Rv419SP6.seq:.....
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GGACACCAAAACGTCAAGAACTACGACGGCAGTTGGACAGAATACGGTCCCTGGTGGGCGCCCCGATCGAGTTGGGA
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.....Rv419T7.seq:.....
TTTCGCCACCGCNAGGTGCTGCGGTTCCAGAAAAGCGTGTTTCGCCGGGCGCGAGGATTGCACGGTCCAACCTGACC
AGCCGGTCCCGCCACCGTTAGGCAGGATCGCGGTGTCTATATGTTCCGCCCTCGGCATAAACGCCATTGCTGCGGTGA
AAATCGGACATCTCGCCGATTGCCACGTCTACATGATCCGCTTGTCCCGCGCCGGGTGCTTGACAAACGCGATGTCN
GCCTCCTGGGAAGCGGTGGC

Clone Rv41

.....Rv41SP6.seq:.....
TCGCCAAGTGGATTCTGTGCTACCNACGAGATCCGTGGTCCGATCCGCNGCTGCGGCGGGCTGCGACCCTGCATCTCG
GCGGCACCCGTGACCAAATGGCGCGCGCCGAAGCAGACGTCTCGGCGGGACGCCACGCCGACTGGCCGATGGTGCTGG
CCGCGTGTCCGCNCGTNCNCGACCCCGGCCGATCNACCAAACCGGCCCGCGTCCGTTCTGGACCTATCCACGTGCC
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GGTGGCGGCCGCGCCGT

.....Rv41T7.seq:.....
GTACCGTCACCATGATCGCCCCCATCGGCATCGGTGAGCTGATAGATCCCAGCCGGTTTCGCCAACCCCGGAGCGATC
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CCGGACACNTCGAGGGGGTNCNTCAGGAGNCCGGGCGCCACCCGAGGTAAGCCTCCGCCCAGCCTCACACCGCGACCG
GGTATCNCAAGTCGCGCAATAANCCACCACTCCTCGGACCCACGTTGTATGCGGCTGGGT

Clone Rv42

.....Rv42SP6.seq:.....
ATACTCAAGCTTAGACCTCACTGATGTGGCGGGACGCGGGAGATAACCGCGGTTTCGAGCCGTTCAACAGTGGTGGTTC
CCACACCAGTTGTTTGCCTTTGCGAAGTAAAGCGATTTCGATTTGCTCGAAAAGAGGGCTGGCTGCTCGTGAGGGACAT
CCATGGCCGATACCTCAGCGATCTCAACGGTCAAGCGACTGCATGTTTGGCGCAAGGTATCGCTAAGCATAGGTTTCGT
GACGGATTTGACAGCAAGAGCTTTCAAAGATTGCTGTCCACATANTGATTTCGCATCTCTACACCTCTTCGCCGGTGC
TGTCAGAGCCATTTCGAATCAGTTATCTCGCTCGTGCTTGGAAANAATTTTCCAGCCTGCGTTGGACAAACCGCGTC
GCCAAAGCGGT

.....Rv42T7.seq:.....

AGCTTCCCGAGAAACAGTGCATTCCCTAAGCAGCCCGTTGTACGCCGATGAGTGAAGAGTGCACGCAATCGCCGGAA
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CAAACGGCAGAAGGCGGCCTCGTCCGGTCCATCTACGCCGAGCACACTGGTGATAGCGCGCATCGGCATCGGTGCGGC
CACGGTGGAGACGACGTCCGCGGGCGTCTGGGTGAGTAACCCGCCGACCAAGTTCTCGGGCAAGCTGGTTCGACCATCGG
GCGCCACGTCTCAACGCGCCACGCGCCATACCTGGTGCCAGTTGCTTGCATCGCGGTGTGCGCCGGCGGATCGGA
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Clone Rv43

.....Rv43SP6.seq:.....
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CGGGTCGTACTCGATGTGCGCGACCTTGGCGTTGACACCATCTTTGTTCATGGCGGCGAAAGTCGATCATCCGGTAAGC
GCGCTTATGACCGCCGCCTTTGTGCCNGGTGGTAATCCGGCCATGCGCGTTGCGTCCACCGCGACCGTGCAGCGGGCG
CACCAGCGACNTCTCCGGGGTTGACCGGGTGATCTCGGCGAAATCAGATACGCTGGCGCCGCGACGACCGGCGTCGT
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GTCCT

.....Rv43T7.seq:.....

TAGCGGTGTAACCAACTCCCGGGTCACCACCCGCAAACCTCTTGCGGCAACAGCACCGTCGACGCGTCAACCGGGCTG
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GATGCACCACAAATGACGGCCGCACACCGGTGGGGACGGCCAGCAGAGCCGTGTGCGCGAAGTCGACGCTAATGC
CGTAGGCTTGGCCGTACAACAGGCGACGCCCCCGGTACCACCGAGTCCACGGNGGTTGGGCGGTCTCCTCGGCCAA
CCAGGCGTGAACCCGGCGGATCCGAATGCAGCAAGACCCGTGGGC

Clone Rv44

.....Rv44-2ndSP6.seq:.....
CCATTGGTTCGGTGTGCGCATACCANTACNACGCGCGGGGCACCTGACGCGGCGGCGCAACCATTCGGTGGCCATCGC
CATCGTCTGCCGACCGGTCAACGGACGACCTTCTCTGGCCGACCTAGTGCGCCACCCGCGCGGTTGCGTCCCAT
CGATCCGGTCAACATGAGCAGCGCCAACACCGAGCGGTACATGACATCTGCTGTGGAACAGTGACANATTCCGCCGC
CCATGATGATCNTCGACCGTCTCCGGATTTCGGTC

.....Rv44-2ndT7.seq:.....

GCCGGCCTGGTCAAAGGGGCGTCCGAAGGANCCGGGCTGGGTAACAAGTTCCTGGCTCATATCCGCGAATGCGACGCC
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GAGGTCGTGAGACCGAGCTGATCCTGGCAGATCTGCAAACCTGGAGCGGGCCACGGGCCGGCTGGAGAANGAAGCN
CGCACCAACAAGGCGCGCAAGCCGGTCTACGACCCGGC

Clone Rv45

.....Rv45SP6.seq:.....
GATCCACTGACCAGATGACATATCGAAATGCTCGACGATTCCGATGGCGATCAAGGCCACGATGCCCTGGCCGTTGG
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CGTCGGCACGCATACCCCGCCGNTGCCCGGAGTGCGCCTCGAGTTTGGCGGCCAGCTCTCCCGGTAGAACTCTC
ACCGTTGGTTCGCCGCGATCTTCTCTANCGTCGCCGCGTGGTCAGGAAAGGTAAACAGCTACCGGGTTTCGGCGCTCG
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.....Rv45T7.seq:.....

TCTACTGCCGAATCGGGGAACGGTCCTCGCCACCGGTTTCGTGTTGCCGGAATTACTCAGGACACCGAAACGTGAG
AACTACGAGCGGAGTTGGACANAATACCGCTCCNNGTGGGCGCCCCCATCGANTTGGGAAGCNGAAATGTGCTCTGG
ACCCACCCAAGAATGACATTGCCGGCCGCCCTCCAACCTGGAAATAGAAACNGTGATCACCCGCCGCGTTCTTGAAG

GAATGGCATGCCCTGGGCCGGGCGTTCCTTCCGCTGCCGGACTCCTCCCACCAATTCACCGCCGAAGGCGTCCCGTCT
GC

Clone Rv46

::::::::::Rv46SP6.seq::::::::::
ATACTCAAGCTTCTGTCAACGAAATCCCGCATGGGATAACGGGTTTAGATTTGACAAACGGGACCGTGTTTCTCAACA
AGCCGGTCATCAGCTGGGCCGGCGACAACGGTATCTACTTCACCCGCTTTCGCCCCGT

::::::::::Rv46T7.seq::::::::::
CTGGCTCAAGCGCTCGGCGCGCAGGTGAAGTACGGACCGGCTCGACGTCGCCGAACGCGAGGCGGTGCTGGCCCACGCC
GACGCCGTCGTCGCACATATCGGCACCGTGCACAAGTCTACAACAACGCCGGCATCGCGTACAACGGCAACGTCGACA
AGTCGGAGTTCAAGGACATCGAGCGCATCATCGACGTCGACTTCTGGGGCGTCTCCACGGGGCC

Clone Rv47

::::::::::Rv47SP6.seq::::::::::
CCGCCCTCCGCATTATGGGTCAAGAACCATCGGGTCGGACTTCTGGGCTTCCAACGCTCGCGCCGTCCCN

::::::::::Rv47T7.seq::::::::::
CCGTGGCACTGTCAAGCATATGCGCCGCTCCTCCTCATCGCTGCGCTCGGCATCGTCGCCGGCGGTGTCGGCGTCACC
CTACCCAAGCCGAACGCGAAACGAGAAGTGTCCATTATTAGGGTGTGAGCACCATAACAGATTGCTCACCAGGAA
CTCAGCGAGCACCGGGACGGATGTGCGCCACCACGCCCATCTGGGGTGGTAGCGGGGAAATACCGCTAACGCGGCTCC
GGTGCCG

Clone Rv48

::::::::::Rv48SP6.seq::::::::::
TACTCAAGCTTGTCCAAATATCGAAGCGTCGGGTGCGGAGGCTCGGTGCGGCAGCTCCAGCAAAACCCGCTCCACCCCT
AGATGCCGGTATCCCTCAAGGTCTTTATCCGCCGCTTACCCCACTGGCACACGGTCACCGGCAGTCGCCCCCGGCC
ATGGCGCGCAACCGCTGAAGCGGACCCGACAGCCGCTGCGGTGATGGACTGATCGCGATCCACCCGGCATTTAGCCGG
GCTATCCGCGGGAAGTTCGCCGGTCCCCCGCCACATACAGCGGAGGATAGGGGCTTGTACCCGGCTTCGGCCAGCAG
TAGATCGGATCGAAGTCCACATATGTCCCATGGAATTCGCCCTGCTCCTGCGTTGAGATCTCGATTATCGCGCGCAAC
CGTCTCATCGATCACAGTCCGCGCACCCGAGGGTCCACACCATGTTGGCGACTTCTTCGCGCAACCAGCCACACCCA
CGCCGAAACGAAACCGTCCCTGCG

::::::::::Rv48T7.seq::::::::::
CAGGCATGCAAGCTTGGCCAACTCCTCATCGGACTTGAAGGTGCCGTCTCTGTTGGCGGGCCCTGCTCCACGGCACGTT
GATGGCACAGGAATGTGTCCGGGCCGCTGGCTTTGTTCTGCGGCAGGTGCGCGGGGGCCAGGATCTTGCCGGAGAA
CTCGTCGGGAGAGCGCACGTCGATGAGGTTCTTGACGTTGATGGCCGCCAGGACCTCGTCGCGGAATGCCGAATCGT
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C

Clone Rv49

::::::::::Rv49SP6.seq::::::::::
ATACTCAAGCTTCAAAACAGGCCTGTTGTGGGCGCACCCGGCTCGCCGAGTTCTGCACGCACCGCCTCAAGTGCGGCC
CGCACCGCCGGCATCTCCCGGTACGCAGGGCCGCGGCCGCGCAGCGACGGCGTGTTCGCGCAGTTTCGCCGTCA
ATGATGCTGACCTGATCGGCCACCCGGGCGGTCTCGGCGTCTGCCGTTCACTAATCGCGGTGCTCAGCAGCGTCTCG
ACAGCCACCAACCGAGTGAGAGACCAGATGCNCCACCACGGACCGCAGCGATGCCAGTCACCTACCCGCTCC

::::::::::Rv49T7.seq::::::::::
CAGGCATGCAAGCTTTGCAGTTGCTGAGTAATGTGGGCCAACGTCACCACAATCGCGATGAATTCAATCATGCCGCC
AGGGCGGCCAACCAATGGTGGCCGCGAGCGGCAGCTCGATCGCAGCGCGGAGGTTGCCGGCCGCGAGTTGATTCAG
AACAGGGTGAGGTATAGGCGGGCAGGATAGTGACGAAGGCAAGACCTAGATCTGCCGTCGGAAGAAGAATCGAGTAT
CCGGTCGACACAACGGAAGCGAAAGTGTCCGCGATGTTGATGAGCGTCGCCGTTGTGGCGGGGTGGCGGCGGTAGC
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ATCT

Clone Rv4

.....Rv4SP6.seq:.....
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CTTATGCAATGCTAATTCGGGGCAAAGTTCAAGGCGGATCGGCCGATGGCGGGCGTAGGTGAAGGAGACAGCGGAGGC
GTGGAGCGTGATGACATTGGCATGGTGGCCGCTTCCCCGTGCGCTCTCGGGTAAATGGCAAGGTAGACGCTGACGTC
GTCGGTCGATTTGCCACCTGCTGCCGTGCCCTGGGCATCGCGGTTTACCAGCGTAAACGTCCGCCGGACCTGGCTGCC
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.....Rv4T7.seq:.....

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GCCGAGTGCGGGCGCTGATTCTTTCATCGAGCCAGGAGGCGCATTCGTGTTTCGGCCGCTGCGGGTTCGGCCCCATCGT
CGACGCGATCCGTACCCACTCCTCGATCAGGTCTGCCTCATCGAACGGGCCAACGGTGCTGTCGGAGTAAGTGTCG
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Clone Rv50

.....Rv50SP6.seq:.....
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.....Rv50T7.seq:.....

AGCTTCCGTACGACCCGCCCTCGCCGGTGCCGGCGCCATCGGTTCATCGGATCTCATGACGACGTCACGTAGGCCCGC
TAGCCGCGAGCGGGCGCGGTCAACTGGCGAGGCGGGCGCGACGTGACTGAGCTGGCCGAGCTGGACCGGTTACCGCG
GAACTACCGTTCTCGCTCGACGACTTTCAGCAGCGGGCTTGACGCGCGCTGGAACGCGGCCACGGTGTTGCTGGTGTG
CGCGCCGACCGGCGCTGGCAAGACGGTGGTCG

Clone Rv51

.....Rv51SP6.seq:.....
ATACTCAAGCTTGCCGGGACCGCGGAACAGAACCGGCGGTTCTTACCGCGGTGTGCGGCCGGCGCGATATCGGCCTCC
CGACTAACCGAACCCGATGTGGGCTCC

.....Rv51T7.seq:.....

ACGTTGGCTCTGCCGGAACGTATTTCCAGCGGCACGCATTCCGGCGTGGGTGCCGGGCGCCGAGTTGCGTCGCTGGGAT
CACGCAGCAGTCGCCGGCGGCTGCCGTGGGCTATGAATTGCACCGAGCCGGAAAAATCCNCAC

Clone Rv52

.....Rv52SP6.seq:.....
ATACTCAAGCTTGTCGTATTCCGTGGCACTGTCAGACATATGCCCGCTCCTCCTCATCGCTGCGCTCGGCATCGTCG
CCGGCGGTTCATGGCGTCACCCATACCAAGCCGAACGCGAAACGAGAACGTGTCCATTATTAGGGTGTGAGCACCAAT
ACCAGATTGCTCACCAGGAATCACGCAGCACCGGGACGGATGTCAGCCACCACCCCATCTGGGGTGGTAGCGGGGA

.....Rv52T7.seq:.....

CGTTGGTAGCCCGATATGCATAGTGTATCTTACTGAACATGATTTCCATTATGGAGCCCGGGGTGCCGGCAGCGCGAA
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GTACCGGGCGACCCACCGCTTCGAGGTA

Clone Rv53

.....Rv53SP6.seq:.....
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GTCGGGAGAGCGCACGTCGATGAGGTTCTTGACGTTGATGGCCGCCAGGACCTCGTCGCGGAATGCCCGAATCGTGTT
ATCCGGCGGGGAGGCGGTGTATGAGGTCACCGGCCGGCTGACCGGGTTCGCTGGACAGCGGGCGTCCGTCCAGTCCCA
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.....Rv53T7.seq:.....

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GAAGCGGACCCGACAGCCGCTGCGGTGATGGACTGATCGCGATCCACCCGGCATTGAGCCGGGCTATCCGCGGGAAGT
TCGCCGGTCCCCCGCCACATACAGCGGAGGATAGGGCTTTGTCCACCGGCTTCGGCCAGCAGTAGATCGGATCGAAGT
CCACATATGTCCCATGGAATTCCGCCTGCTCCTGCGTCCAGATCTCGATTATCGCGCGCAACCGCTCATCGATCACAC
GTCGCGCACCCGAGGGTCCACACCATGGTTGGCGACTTCTTCGCGCA

Clone Rv54

:Rv54SP6.seq::

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GCCGCCACCGGAATCGGCCAGCCGACCGAATGGGCCAGCGTTGCCAGCATCAGTCCGGCGCCGGCCGACACCAAGTGA
CGGCAACGGTGAAATCGCGTGGGCGGCAACGCCGGTGAACAACGCGCGGGCATCTCGCCCCGACGACCGCCAGGC
AGGGGTGCCCTGGGCCAGCATCCGACGCCGAGACGACGAGGACCGAGCCAGTGCAGTAGGCAAAGACCGCTTGTGCGA
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:Rv54T7.seq::

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CGACCGCTAGTTGCGGATCAGAAATCCGTTGGGCGCGGAAGTCCAGCCGAATTTGTTCTCCCGCTCCGCATCATGCTT
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Clone Rv55

:Rv55SP6.seq::

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CCAAACCGGGGACAGCTCCCAATTGACGTGAGCCCGCTCACTTGCTGGGTAAGCGTCG

:Rv55T7.seq::

TAGCGCCCCCTCCGGGCGGAGCTCCACGGCGTGATCAAGGTACCGGCCGGGATGTTGCGCAATGGCAGGTTGTTGC
CCGGCTTGATGTCGGCGTTAGCGCCGGATTCCACCACATCCCCTTGCGAAAGTCCGTTGGGTGCAATGATGTAGCGCT
TCTCCCATCGAGATAGTGGAGCAACGCAATCCGTGCGGTACGGTTCGGGTCGTACTCGATGTGCGCGACCTTGCGCT
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TAATCCGGCCATGCGCGTTGCGTCCACCGCGACCGTGCAGCGGGCGCACCAGCGACTTCTCCGGGGTTGACCGGGTGA
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Clone Rv56

:Rv56SP6.seq::

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CCGCGTCGCGGTATTGCGGGTTGGTGAAAAGGCCGATGCTGCCGTTGCCGCGGGGGCGGATGTTGTGCGGGAGTGACGA
TCTGATCGAAAGGATTAGGGCGGCTGGCTGGAATTCGATGCCGCGATCGCGACACCGGATCAGATGGCCAAAGTCGG
TCGCATCGCTCGGGTGTGGTCCGCGCGGCTGATGCCCAACCCGAAACCGGCACCGTCACCGCCGACGTGCGCCAA
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:Rv56T7.seq::

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GTTGCGTCCACCGCGACCGTGCAGCGGGCGCACCAGCGACTTCTCCGGGGTTGACCGGGTGATCTCGGCCGAAATCAGA
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Clone Rv57

.....Rv57SP6.seq:.....
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GCTGTAATAGCCCAGGGTCGCCACGCTTCCATCCGGGCCCCGACCCGGC

.....Rv57T7.seq:.....
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CGCACCGACAGGCCGAACCCGCGGCCCGCACATGCCCGTTGATGGCGCCGACCACCGGCAGCGGCGACTCGACGAT
GGCGCGCAACAGCGCCGTCATTTCCCGCGCCCGCGCCACCGCCATCCGGTACGGATCACCACCACCTCCGCCGGCCTC
GCTGAGGTCC

Clone Rv58

.....Rv58SP6.seq:.....
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CCAGCCCCCGAATCCGGTGACACAGGCGACACCCCGGCCACACCCGGTATCGACGGCGCGCTGCTGTTGCGGCTGTG
GCCAGCTCGCAGGACGCGCTGCGGCAAACCGCCGCGCGGTGGCCGATTGGGTCT

.....Rv58T7.seq:.....
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CATGCTGGTTGGCTGTCTTGGGACGATCCCGAAATAGTCCACGCGGATCTGGTGATTTTTCGGGGCTACCCGCGATTAC
CCCGCGCGGCTCGACGAGTTTTTGGCCTGGACTACCCGCGTGGCCAATCTGCTGAACTCGCGGCCGGTGGTGGCCTGG
AATGTCCANCGCGTTACCTACGTGACCTTGATGGGATCCGGGGNT

Clone Rv59

.....Rv59SP6.seq:.....
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CGGCGGACGGCTCGACGAGCTGGAACCTCAGCGACGACGATCCGGAATTGATCACCAGCACGGTGCTACTCATGGACC
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GAGCAGCTCCTGGGCGATGGCCAGGTTCTCATCGATGGGCACTGCCGACCGTCCACATGTGCGACGGAACAAAGATG
TCACCTTGCTCACGCGTGCGCNAGATCNCANAAGGCCGGACATACTGTCTNACTTGCTCCTTGGGCGAGTGGTCCGTGTC
AGCCCACGTGACGGGTACTTGGCGCGATAACGTGGT

Clone Rv5

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ACCACACCGTGACGGCGCCGAATTCGTCAAGCGCGGTCTTGATGATGTTGCTGCGCCGTCTCGGTGGCGACGCTG
TCCTTAGTTGGCGACCGCCCGCCCCCTTGTGCGGAATCTCGGCGACGACCTCATCGGCCATCGCCGAACGGCGCCC
GTGCCCCGTGCGGGGCGCCACCGAGGTGCTTGACCACGA

.....Rv5T7.seq:.....
CAGGCATGCAACCTTTGTCCACACGGCGTCTACTCCGTGCAAGGTCCGACCGCTTCCACGTCCCGCCGTGACGGTGCT
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Clone Rv60

.....Rv60SP6.seq:.....
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AGGATTGCGCGAAAAACGTCTACGTGGCGGGTGTACTGGGTGTGCAATGATTCTGTTGGGTGCGTATGCGTCTGCAAT
CGTCGACATAGATCCGTGCGCGCATCGCGTCGACAACCTCCGGGTGAGTGGAATACACTTGCCGATCACGCGACGTGCG

CGGATCGATGCCGACCGAAATACGACCACATGGCTCTTGTTCNCAGTGTGGCGGCATCAAATACCCTCAGTGCCGT
CCGAC

::::::::::Rv60T7.seq::::::::::
TTNCCGCCTTNACGCCTACTCCNAGACGATGCTCGACGCGTGTGAGCACACGGCGCTGCTGTAGACGGCACGGCGCAG
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GCGCAGAGTGTGCATGTGCGGCTCTTGTGAACGAACATAGCAAAGCGTATATGTCTGTGGCGGCTCTGCAGATATCGC
GATAATACGTATATACATAAGGTGGCGCGCATCTATCGGTATATCCGTTATGGCGGACGTGCGTGAGCGTGAGTCGC
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Clone Rv61

::::::::::Rv61SP6.seq::::::::::
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ACGGCGAGCTCGATGCTTGTTCGAAGNGCGCANGCGGTTTCGATCTTGTCCGCGTCAACGCAGATCGGATCTCGCC
GCGGTCTGCATGACGATGGGCGCAGGCCCGCTCATGTCCCGTAGACGGGGAGATACGGGCAGCCGCGGATCGAGACCT
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::::::::::Rv61T7.seq::::::::::
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GCCTCGGAGTCCGGCCGAACAATGGCCATTTCCCGGACTCTAGAATCCAGTCATCGTCTCGGTGACGACGCCTTGCC
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Clone Rv62

::::::::::Rv62SP6.seq::::::::::
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::::::::::Rv62T7.seq::::::::::
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GCAGCATGAAGGTGCGCGCCCGCACGATGTGGGCGAAGCAACAGGTAATAACTGGTCGGCATGGGTCAACCCCTCATTTG
GGCCGTTGCGGATCGGGTGACGCCCCGAGTGCCGGTGGAACTCAACACCGCCTTACCGATCTTTTCGTGAAAAATG
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Clone Rv63

::::::::::Rv63SP6.seq::::::::::
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GACTTGAACGACCTGTACCGCAGGGTGATCAACCGCNACNNNGNTGAAAAGGCTGATCGATCTGGGTGCGCCGGAA
ATCATCGTCAACAACNAGAACGGATGCTGCNGGAATCCGTGGACGGCGCTGTTGACAATGGCCGCCGCGCCGGCC
GTACCGGGCCGGCAACCGTCCGCTCAAGTCGCTTTCCGATCTGCTCA

::::::::::Rv63T7.seq::::::::::
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GGCGTTGACACCATCTTTGTCATTGCGGCGAAGTCGATCATCCGTAAGCGCGCTTATCGACGCCGCTCTGTGCCGG
GTGGTAATCCGGCCATGCGCTTGCCTCCACCGCGACGTGACGCGGCGCACACCGACTTCTCCGGGTGACGGGTGATC
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Clone Rv64

::::::::::Rv64SP6.seq::::::::::
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CAGCGCCGTGCGCGCCCGCCCGCTGCGGCATGCTCACATAACACCTCGATCGCTGCGGGAGTTGCTCGTGGCCGAC
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.....Rv64T7.seq:.....

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GCGCTGGATGTGTTGTGCCGCAACGGAATCCCACCTCAATTATGACCTCGTTGTGGGCGAGCGCGGTATCGTACGCCC
GACCAGGAATCGTCGATGCTATCTCACGTACCCGAAGGCCTCTCCCAGCACACCGCATCCAGAACGTGCACACNGTCG
ACATGTCTCGGCGGATCCGCCTGCAGAACGAACGCCANGTGCGCTGTGCGACACGGGTGCGGATCACCGCTCGCACGC
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Clone Rv65

.....Rv65SP6.seq:.....

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CTGTGCGCAGGGGCCCTACCGCCAACCCGTGCGGGGTCTGCGAATCCTGCGTTTCGTTGGCGCCCAACGCCCCCGGCAG
CATCGACGTGGTAGAGCTGGATGCCGCCAGCCACGGCGCGCTGGACGACACCCGCGAGCTGCGGGACCGCGCGTTCTA
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.....Rv65T7.seq:.....

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GCTGGCCGGCATGGTGAATCGACCAGCAGCTCAACCCGTACACCAACCCCGACGGCGCGCTGGCCCGCGGGAACGT
GGTCTCTGACACCATGATCGAGAACCTTCCCGGGGAGGCGGAGGCGTTGCGTGCCGCCAAGGCCGATCCGCTGGGGGT
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Clone Rv66

.....Rv66SP6.seq:.....

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GCGTTACTGCGGTGACGGCTGTTAAGCGGTTACGTACCTCCACGGCACTCAAGGAATTAAATCCCGAATCGGCAAACG
CCTGGCCAGCGTCGAATCCGGCAGCGCCGTGCGGCCCCAGCACCGCTGCGGCATGCTCACATAACCACCTCCATCGCTG
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.....Rv66T7.seq:.....

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AATTGTGCGGTTGCCCCGCAACGGTGAGGTGCTGGTCNGCCAGCCCGCCAAGAACAGGCAGTGACCAACGTCGATCGC
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TTCAATGACCCACGTCNGGCACCAAGGACCCGGCAATCGCGGCTCACTTGNCGCATNGTCNACAACCAACGCGNCGC
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Clone Rv67

.....Rv67SP6.seq:.....

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CGGCTCACCATTGTTGACAACTTCGGTGGCCGGATCCCGTCGGACAAACCGCCCATCAAGACACCCGCGAGCTCGCG
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.....Rv67T7.seq:.....

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AAGAACCTGGTCGGCATGGGTGAGCCCTCATTGGGCGGTTGCGGATCGGGTTGCAGCGCGCCGGAGTGCCGGTGCAG
CTCAACACCGCCTTCACCGATCTTTTCGTGAAAATGGCGTCGTGTCCGGGGTATACGTCCGCGATTCCACAGAGGCG
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ATGCGAAT

Clone Rv68

.....Rv68SP6.seq:.....
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GTCAGCCGCATCCACTGGATGCCTTCTCGGNGTTTCAATCANGTACANGCGACGTTTCGCCACCATCGTGCCGGGGCAC
GGTTAGCGAGAAACCGCCGACTTCACCGATTGCGTCCGTCGATGCCGTGCAACAGATCGGGCCTATTGTGACAGCCAG
TGTGATNCGTATTTGCCGCCGTGCTCCTCGTCGCAACGATGCGAACACAGATCCGTGGNGGACGATAGCGGCTGACAA
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.....Rv68T7.seq:.....

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CCTTGGGTCTCCGGTGGTGCCGANGTGTANATAAGCTCCCGGGTCCGTCAACGTANTGCGCAGGCGGGCGGTTACTCGG
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TCGGCACATGTCCTTTGATCGTTTCGAACAN

Clone Rv69

.....Rv69T7D3.seq:.....
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NCTTGTGCAGGTGTTCCGGCAGTAGCTGCTCGGAAAATCGGCTGGAAACCGCATCAATGGTCGGTCCAATCGAACCG
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Clone Rv6

.....Rv6SP6.seq:.....
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.....Rv6T7.seq:.....

CAGGCATGCAAGCTTGTGCTATTCCGTGGCACTGTCAGACATATGCGCCGCTCCTCCTCATCGCTGCGCTCGGCATCG
TCGCCGGCGGTTCATGGCGTCACCCTACCCAAGCCGAACGCGAAACGAGAACGTGTTCCATTATTAGGGTGTGAGCACC
AATACCAGATTGCTCACCAGGAACCTACGCAGCACCGGGACGGATGTCAGCCACCACGCCCATCTGGGGTGGTAGCGG
GGAATACGGCTAACGCGGCTCCGGTGCCGGCAGCCAGCGCAGACCCTCGGCGGCGGACACGGCTAACAAACGACGAC
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Clone Rv70

.....Rv70SP6D2.seq:.....
NCTACGCTGCTGAATGTTGTGCGCCGGAGGANCTCAAGACCCACGCGGTTGTACGCGGACNTGCGACATGTTCAACCG
CCGGA

.....Rv70T7D3.seq:.....

CTAACCAACAAGCCATGGTGGTTGGCGCCGTGAGAGGTGCGCGGTGCCACAACGGGAAGATCGCCTTGAGCGTCGC
TCGACCGCCGCTCGAGTTGGGTGATAACGAAGTACTGATGCCGATCATGTCGACGTGTCCGTGCGCATCAGCGTGCAG
CGGCGACCCCTCGACGAGCCTCGGTGCCGCCGCGGCCAGGGCACCAGCTGTTTTAGCGCATTGTGCTCCGCCGGTAAT
AAAGGANGTCGGTCGCCTCCGCTGCTGTGGTTGCGGAATAACATCTTCCCTTCTGCAACAGGATGAGAATGGTTTA
ATTGCTC

Clone Rv71

.....Rv71SP6.seq:.....
CTAAGCTTTCCGGTCCGCCGCCACTAGTACCGCGTTGCCGGCCCCGCCGACCTAGAATGTTCCGCCCATTGCCGTTTC
CTCCCGCCGCCGGTT

.....Rv71T7.seq:.....

TCTGGTGCCGGGTGTGCCGACGGGTCCGTCCGCCTCTGCTTCAGTGATTCTGTGATGCGACCGGCAACGTCCTCGTTG
TTCGGTGTCTATGTGGTCCGTCTCTCCTTGTTCGCATACGATT

Clone Rv72

.....Rv72SP6D2.seq:.....

GCGATCGNTNACCACAAGGGCGCAACCGTTCGCGCGTTCGACTGAACGTGCTGCCGCCTGGAGAACTGGCGCTGCTGCC
ACCTGGTCGGCGCATCGGCACTTCGAGGACTGGATTTCGACGCGTGGCCCCGACCTGANGTNGGCGGTGGACNNGTGTG
CACCCGGTTGATTCTCGGCCTTGCCGGGATGCCACCTGCGCCTGGTGGTCGAT

.....Rv72T7D3.seq:.....

CGTGACCGGACGGGGTGCCGCGCAACCGGTCTTGGCCAATTGCCGGGGACTGGGGCTGGAGTATAAAGCGGGCCTGT
TGCCGGAAGATAAAGTCAAAGCGGTGACCGAGCTGAATCAACATGCGCCGCTGGCGATGGTTCGGTGACGGTATTAACG
ACCGCCAGCGATGAAAGCTGCCGCCATCGGGATTGCAATGGGTAGCGGCACAGACTGGCGCTGGAAACCGCCGACGCA
CATTAACCATAACCACCTGCGCGGCTGGTGCAAATGATTGAACTGGCACGNCCACTCACGCCAATATCCGCCAGAAC
TCACTATTGCGCTGGG

Clone Rv73

.....Rv73SP6.seq:.....

ATACTCAAGCTTCTTACCCANAGCATGAACCCCGCCGTCCAATGCCGCCACCGTGGTGCTGTGCGCCGGCCGGGTGCG
GGCACAATCGCCGAGTTCGGCGAACAGATCCTCGAAGGTCTTCACGGCCAGCGATTGTTGCACGTGTGAGCCAGCCAA
GTACGGTGGTTTGACGCCACACGTTTCGCCACCGCCGCGCGCGCATTAGGGCATCCTAATATAGGTTAGGCTACCTT
ANTTATTCTGTGGTCNAAGGAGGCAGCCGAACGTGACCTTCCCGATGTGGTTCGCAGTTCCGCCGGAAGTGCCGTCA
GCATGGCTGTCCACCGGCATGGGCCCCGGTCCGCTGCTGGCCGCGGCCAGGGCGTGGCACGCGCTGGCCGCGCAATAC
ACCGAAATTGCAACGGAACCTCGAAGCGTGCTCGCTGCGGTGCAGGCAACTCGTGGCAGGGGGCCAGCGCCGACGGTT
CGTCNTCCCATCAACCGTTCCGTATTGGCTAACACCTGCACGGTGGCACCGCACAAACGCCGCCACAAACGCGCCCC
GGTATAC

.....Rv73T7.seq:.....

GGCCGAACCTAATCGGTTGTTGGCGGCTGCCGAGTTGGGTCACTCGGGGGGTGTGCACTGGCACATGGTGGGCGGAT
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GCTGGATCGGGCGGTTGTTGCGGCGCTGGCCGAACACCGTCTGTCGAGCGGCTGCGGGTTTACGTCCAGGTGAGCCT
CGACGGTGACGGATCCCGGGGCGGCGTTCGACAGCACGACGCCCGCGCGCTAGACCGGATTTGCGCGCAGGTGCAGGA
GTCAGAGGGCCTCGAACTGGTTCGGGTTGATGGGCATTCCGCCGCTGGATTGGGACCCGACGAAGCCTTTGACCGGCTG
CAATCGGAGCACAAACGGGTGCGTGCGATGTTCCCGCACGCGATCGGTCTGTGCGGGGCATGTCCAACAACCTGAAAT
CCGTCAACATGGTCGAC

Clone Rv74

.....Rv74SP6.seq:.....

GCTTCCCCTGATACTCGACCAGCCCCACTCGGGCCAATACGTGAATGTCCTAGCATTTTTACCCGTTACGGGCTAG
TCGAGTAGTAGACGATTGATTAGCCTGAACGTACCTCCGACGGCCAGCTGACGAACGGGTTTGACGGA

.....Rv74T7D3.seq:.....

TCAGCTGTCTGTAGAAGGGCTGGCGATACTGTGCACTGTCTGATATCGCNCNGTNGTGGGACTATNCAGNCCATNANG
ATGCGGTTTCNGNNNTGCAAGNATCCTGGNACACATNCGGTTACGTTAATCANCATCGCGANTTNCNCGTNTTCG
ATTANTTCTGCTAACGNNTCTNNNAGTGCCTGCGGGTTCGACTCTAGAG

Clone Rv75

.....Rv75SP6D2.seq:.....

NCTCTGCCGGGCGNAGAGCGCAGAGTCGGACGGCTTCGTGATCGTGAAGCGACCNCTGCGATGANAGATATCGNTNAC
ACTGCTCANAACTTCGGATCATCGNTGATACACAGGCCAACGGGTAGCGGTTGTCCAACCGCTTCGTCAACGANATG
GGATCGTGACGANCTACGCTCGCAGGATATGTCGCNGACCNNGTCTAGANAN

.....Rv75T7D3.seq:.....

CACTTCATGCTCGTGCGTTGGCNCATGATTTGCNCGAGNGGTTAGCTCCTCGAGTGNGTGACGTATCACTCCGGCNGAC
TANCCGTATCNGCGTCCCGCACCGGTCAACTGGTCTAGCCACACCGGGGAGAAATNCNCGACCGGNGCTATCGACCNAT
CACGGCTTGTCGNNAAGATAGNCAGCC

Clone Rv76

.....Rv76SP6.seq.....
ATACTCAAGCTTGCCAACCGCCACCCTGCATCCGGGGGGCGAGCACTGCTCCGCCGACCAGTACGAACCAACCTGCGG
TGCCAGGCCATTGACAATGTGCTGGTCGGCGCCCGCGAGTTCTAGCACAGCAACGCCGCGGCCACCACAGGGGCG

.....Rv76T7.seq.....
CGGTCGGTGTGCTTGGCGGCGTGGGTATCAACACCGCCACGAAATGGGGCACAAGAAGGATTGCTGGAGCGGTGGC
TGTCGAAGATCACCTCGCCAGACCTGCTACGGGCACTTCTACATCGAGCACAACCGTGGCCATCACGTCCGGGTGT
CCACACCGGAAGACCGGCGTGGCGCGGTTTCGGCAAACTTTGTGGGATTTCCCGCCCCC

Clone Rv77

.....Rv77SP6.seq.....
AATACTCAAGCTTCGCGGAGGTGGTGGGGCAGGAGCACGTCAACGCCGCGCTGTGCGGTGGCGCTGGATGCCGGCCGGA
TCAACCACGCGTACCTGTTCTCTGGGCCGCGTGGCTGCGGAAAGACGTGTCAGCGCGTATCCTGGCGCGGTGCTTGA
ACTGTGCGCAGGGCCCTACCGCCAACCGTGCGGGGTCTGCGAATCCTGCGTTTCGTTGGCGCCCAACGCCCCCGGA
GCATCGACGTGGTAGAGCTGGATGCCGCCAGCCACGGCGGCGTGGAGCAACCCCGCGAGCTGCGGGACCGCC

.....Rv77T7.seq.....
GATGGCACTCACGCTGGACAAGACCTTCAAAAATCTGAAATCCTGACCCGATACTTGAACCTGGTCTCGTTCCGGCAA
TAACTCGTTGGCGTGCAGGACGCGGCGCAAACGTACTTCGGCATCAACGCGTCCGACCTGAAATTGGCAGCAAACCG
GCGCTGCTGGGCCGGGCATGGTGCAATCCGAACAAGCACGCTCAACCCGTACACCAACCCCGAAGGGCCGCTGGCCCG
GCGGAACCTTGTCTCCA

Clone Rv78

.....Rv78SP6.seq.....
AACAGCTATGACCATGATTACGCCAAGCTATTTAGGTGACACTATAGAATACTCAAGCTTCTGGGCGTCGTGGTGCCC
GGCCTGCCGGTGCAGGAAGTGGATTTTACTGCCATCTCTCGCGACCCTGAGGTGGTCCAGGCTTACAACACCGACCCA
CTCGTGACACGACGGGTTCCGGCCGGGATTGGCCGCGCGCTGCTGCANGTGGGCGAGACCATGCCGCGGCGANCA
CCGGCATTGACCGCGCCGCTGCTAGTGCTGCACGGCACCGATGACCGGCTGATCCCCATCGAAGGCAGCCGTGCGCTG
GTCNAATGTNTNGGATCNGCCGACGTGCANCTGAANGANTATCCCCGGCTGTNCCACNAGGTGTTCAACGAACCGGAN
CGCAACCAAGTG

.....Rv78T7.seq.....
CAAGGCATACGCCAAGACCCAAGGGATCGCAGTCACCTCCGTCAACGGCCTGGTCGCCGGCCACGGGTCCGTGCAGGA
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TCCGGAGGTGTTGTGGTTGGCGCANCGCGCAGACAGGCTGGGATGGCGTGCATCGTATCGGGAATGCGATGGC
AACACTGAAGTACGAGCGCATCCTGCGCCAGCATGTTTCGACTACGTCGTCGTTGGCGACGGGGANGTAGCGTT
CACCAGCTGGCCTTGGCCCTGGCGAATGACCTGCGGTTGACGACTCCCGGGACTAACC CGCCGTANTGAGCAAGGAC
AGATTCTGCGCACACCCTCCTCGCTGGTCGACCTTGACA

Clone Rv79

.....Rv79SP6.seq.....
AACAGCTATGACCATGATTACGCCAAGCTATTTAGGTGACACTATAGAATACTCAAGCTTGCCGGTGATCTGGGTGGC
CAACTCGGCGGGACCATCTCCATCAGACNGCAAACGCTCCGGCTTCGGCGACAGCGATCGCGTCTGCGATNGTTTG
TTCGGCGGCGTCTCCGCGGCCCTGCACCCGGAAGCCGCCAAGGTGTTGACNCTTTGCGGGGTGAAGCCGATGTGTGC
CATCACCGGGATNCCCGCGCGGTGAGACANGCGATTTGCTCGGCCACCGCTCACCGCCCTCGANCTTGACNGCATG
TGCGCCGCGCTCCTTGAAGAAACCGGTGGCGGNGGCAACCC

.....Rv79T7.seq.....
CGTTGAGATCCAGCTGCGCACTGTGCAGCGCTCGGTGGTCTGCTCGGCCTGCCGGGATAACTCGTTGAGCTTGGCCA
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TGGCGGACCGCATGATTACACGCGCATCAACCACCTCTGGTCGAGCCTCAAATTTGCTTCTTAAACGGGCCATCG
ACGGATGACGTGAGCTGGTTTAGGTCTCAAACAGGTTACGAAACGATCTCGGAATTGTCCAAAAGGGGAAGTTAAGA
AAATGGATAGATTTCTACCATTTGCTGTGGACGATCGTACTTCTGCTATAGGGCTCCAGGGGCATCGACACGCAACG
ACCTTACGCGACACCGGATCCGCGCTGGCGGCGGAACGGCACANGCGCAACCGAAGGGCCAATCCGACATCGG

Clone Rv7

.....Rv7SP6.seq:.....
ATACTCAAGCTTATCTAGGCGCCAGCTTGATTGGTCTGGTTGCATTGGCCAGCTGCGCGAGCCTGGCTCACTTCAACT
ACAACAACCGCAAACAATTGCCGCCTTCGGATCCGAGTTCGGTTGGGTACGCGGCAATGGANACCATTCTCGGTGA
ATCAGACTATTCCTGAGTACTTGATCATCCACTCTGCACACGACCTGCGAACCCCGCGCGGCCTTGCCGACCTGGAGC
AGCTGGCGCAACGTGTGAGCCANATCCCAGGCGTTGCCATGGTTCGCGGTGTGACCCGGCCAAACGGGGAAACCCCTTG
AACAGGCCCGGGCGACATACCAAGCCGGCCAAGTTGGCAACCGGCTGGGCGGGCGCGTCGCGAATGATCGATGAGCGCA
CCGGCGACCTGAATCGGCTGGCATCGGGTGCCAACTGTTGGCCGACAATCTCGGTGACTTCGCGGTCAAGTCAGCCG
GGCGGTTGCGGGTGTCCGCGACCTTGTCCAGCCCCCTCGCTTACTCCA

.....Rv7T7.seq:.....
CAGGCATGCAAGCTTTTGGAGCGTCGCGCGGGGCGAGCTTCGCCGGCAATTCTACTAGCGAGAAGTCTGGCCCGATACG
GATCTGACCGAAGTCGCTGCGGTGCAGCCACCTCATTTGGCGATGGCGCCGACGATGGCGCCTGGACCGATCTTGTG
CCGCTTGCCGACGGCGACGCGGTAGGTGGTCAAGTCCGGTCTACGCTTGGGCCCTTTGCGGACGGTCCCGACGCTGGT
GCGGTTGCGCCGCGAAAGCGGCGGGTGGGTGCCATCAGGAATGCCCTCACCGCGCGGCACTGCACGGCCAGTGCCCCG
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CCCACGCATGGTG

Clone Rv80

.....Rv80SP6.seq:.....
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GGGCTAGTTGCGTGGGGTGGGGTGATCGAAGATCGCGGTGGCCGGCAGCGTTACTGCGGTGACAGCTGTTAAGCGGT
TACGTATCTCCACGGCACTCAAGGAATTAAATCCCGAATCGGCAAACGCCCTGGCCAGCGTCNAGTCCGGCAGCGCCGT
CNCGCCCCAGCACCGCTGCGGCATGCTCACATAACACCTCGATCGTGCGGCGANTTGCTCGTCNGCCGACCGACCGG
CCANCCGGGCGGCAAACCCNGAAGACCCAAGAATTATCACCAACCATCGCTAGC

.....Rv80T7.seq:.....
CCTTCTTGACACCCACCTCGCCATCGACCTTGAGCACTCCGTCGTAGTTGGTGAACATGTGACCGGCGATCGGGCGGG
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GCGAACCCGAGCCGCGGTGGAACACGAAATCNAACGGCTTGGCGTCNGCCGGCAGTCCGAGCTTGGCCGCGGCCACCT
GTTGCCCTTGCGCAAGGATGTCNGGGCGAANCTTGACGTTGCCGGGCTTGANACGCCATGCACGTTGCCGAACGTCTN
CGGCCAGCANGTATTTGCGGTGCTCACGGCGCCCCANCGCCTCGATGGTTTCTCGAAGTCTCCGGGCTGGTGTACA
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Clone Rv81

.....Rv81SP6.seq:.....
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TCGGCCGAAGCCGCAAGATTGGCCATCACTAGTGACGANATCGTGGCGCTCTGCGAGTANCCNAAGACAGTGACGTTG
TTNCCGGCGGCAATTTGCTGCCGAATCGCACTTTCGAGAATGACNGCACCCCTGCGCCACCGANGAATCNAAGTGAGG
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ATGTNCAGCGCGTTTCGCGANCTCNACATATCT

.....Rv81T7.seq:.....
TCCTGGTGATCGANGGCCGCGGTTCCGGCCGAAAATCCGGTTCGGGTTCCGCGTTCCAACTTGANCGCGGTCC
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CCCCAACCTGATCCAACGACAACCGCCCCCTCCCGCATACCCCGGGCGCAGCGCGGAACTCCGGCAACCGCCGCGCCA
CCGTGGCGATCGTGTGGGCGTTGCCTGACGAACANCCCATCTTCCAGGCCACCAACCCCGCCACCGACCGCGCCCCCG
TCACACCCCAACCCGTCGCGATCCAGCTCAGCCACGATCTCCACAATGCGCCCATCAATCGCATTGCGCTGAACGG
GCAACTCCGCCAACTCCTCCAA

Clone Rv82

.....Rv82SP6.seq:.....
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CATTGAGGCTGTTCCCTGGGGTTCGTTACCTTCCACGAGCAAAACACGTAGCCCCCTTCAGAGCCAGATCCTGAGCAAG
ATGAACAGAACTGAGGTTTTGTAAACGCCACCTTTATGGGCGCAACCCCGATCACCGGTGGAAATACGTCTTCAGC
ACGTGCGAATCGCGTACCAACACATCACGCATATGATTAATTTGTTCAATTGTATAACCAACAGTTGCTCAACCCG

TCCTCGAATTTCCATATCCGGGTGCGGTAGTCGCCCTGCTTTCTCGGCATCTCTGATAGCCTGAGAAGAAACCCCAAC
TAAATCCGCTGCTTACCTATTCTCCAGCGCCGGGTATTTTCTCGCTTCCGGGCTGTCATCATTAAACTGTGCAA

Clone Rv83

.....Rv83SP6.seq.....
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AGCGCCGATTCCACCACATCCCCTTGCAGAAANTCCGTTGGGTNCNATGATGTNNCGCTTCTCCCNCTCNANATAATG
GANCAACGCNATCCGTGCGGTACGGTTCGGGTCNTACTCCATGTNCGCGACCTTGGCGTTGANACCATCTTTGTCATT
GCGGCGAAAGTCNATCATCCGGTNAGCNCGNATGANCGCCGCCCTTGTGCCGGGTGGTAATCCGGCCATGCGCNTT
GCGTCCACCGCGAACGTGCAACGGGGGNCNCAACGANTTCTCCNGGGTTGAACCGGTNATCT

.....Rv83T7.seq.....
TGTGTGTGGTGGTAACCCATCTGAGCAGTGTGCCAAACCGGGGACGCCAGCTCCCAATTGACGTGAGCCCGCTCACTT
GCTGGGTAAGCGTCG

Clone Rv84

.....Rv84SP6.seq.....
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GGGGGTGACGCTGANCCNNGGTGACNTGTTTCNGCTCNGGCACGGTGCCACCTGCACGCTCNTCNAACACCTCANGCC
ACCGGAATCATTCCCNGGCTGGCTGCACGANAGCGANNTTGTNCNCCCTCCAAGTCTAAAGGCTGGGCGANANAAGCAN
AACGTCCCGACNAACGGCACTCCTTTTCCNNTTGTCTTC

.....Rv84T7.seq.....
GAAATCATTGATGGTTTGAATCACCAGGCCGATCAAGCCTTCGCCGAGCCAAATTCCAATCAAGAGGCCCAAGCCCGT
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TATGGCGAAAACGGTCGCCGTTGCACGACATTAAATGTACGGTATTGTAGATTAAAAAGATACCCACCAACAANGC
AATCAAATGAGAGCGGTTAAATTGACCGTAAAAGCGTCCGTCACTGTGTTGACNGTGTCCCGTTGGGTATCCGACGT
TTCCATACGCACACCGGCCGGCAGTCTTTGTTGGATGCGTNTTGAATGGCCTCATCTTTGATGATCAAATCGATGTN
GCTCAGTCTTCCGGGCATATGGAACAACTCTTGGGCCGTGGAAATATCAGCAATGATA

Clone Rv85

.....Rv85SP6.seq.....
CTTTCGCCAGGCCGCGCGGATGTCCTCATCGCTTACGAACATCATCCGAGCTTGACGCTGTGCGCGAACAGATCC
GCGTGC CGCGCGCGCGCGCCACACCGTTGCCGCGATCTGGCCCATCCGAGGTGACCGCGAGCTGGCTGGTCAGG
CCGTGCGAGCTTTGCGGAAGCTCGACATCGTCGTCAACAACGTTGGCGGCACCATGCCAACACGCTGCTAAGCACCT
CGACCAANGACCTCGCGGACGCTTCGCCTTCAACGTGGGCACCGCCACGCGCTGACCGTGC GCGCGGTGCCGTTGA
TGCTGGAACACTCCGGCGCGCGCAGCGTGATCAACATCAGCTCCACCATGGGCCGGCTGGCGGCGCGGGGTTTC

.....Rv85T7.seq.....
TGTGGGCTCCGATCCGGCGCGCATGGCATCGACGGCGACGCCGATCGATGACGGCCAGGCTTACGAGCTTGAGGGTGT
GAAGTTGTGGACCAACGGTGTGGTAGCGGACCTGCTAGTGGTTATGGCGCGGGTACCGCGCAGTGAAGGGCNCCG
AGGGGAATCANCCTTTGTCGTGAGGCTGATTCGCCCGGATCACCGTGGAGCGGCGCAACAAGTTTCATGGGACT
GCGTGGCATCGAAAACGGCGTGACCCGGCTTCNTCGCGTCAGGGTGCCCAAGACAACCTTGATCGCANGGAAGCGACG
GTCTGAAGATCGCGCTGACCACACTCAACGCCGGACGGCTGTCCCTACCGCGATCCAACCGGAGT

Clone Rv86

.....Rv86SP6.seq.....
GAGCTGGCCGAGCTGGACCGGTTACCGCGGAACTACCGTTCTCGCTCGACGACTTTCAGCAGCGGGCTTGCAGCGCG
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CTGGCGCTGGCGGCCGGCAGTAAATGTTTCTACACCACGCCGCTGAAAGCCCTGAGCAACCAAAAGCACACCGATCTC
ACAGCACGCTACGGCCGTGACCAGATCTGGCTGCTGACCGGTGACCTGTGNGTCAACGGCAACCGCCGGTGGTGGTGA
TGACCACCGAAATGCTGCGCAACATGCTCTAC

::::::::::Rv86T7.seq::::::::::

GATCTCTGGATCGGCGGGGCTCTCGGGCCGGCCTCGGCGACCTCAGCGGGCCGCGCCTTCCGGCCGAACCATTCCCT
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CGGGTACCCGGGAGCGCGGGTCNGTANACCANCCTGGACTGCGTCGCGCGGTGCGTCNACNTCAAAGTCCCCGGCGT
CCCATATCGCGTATGACGCGGGCGCGCCCCGGCACCANGGGTGCCGATCCGGCCGTCTCGAACACCACCGGGCCCGCAG
CCGCCGCGGGTCCGGCAGCNAACCCGCCCGCGCCGATAACCCGCTGCCCGCGTGCGTGATTGACCGCCGCGCGCACGCT
GGCCANGGATCAAAGCCCCGTG

Clone Rv87

::::::::::Rv87SP6.seq::::::::::

GGACCGGTAGCCCGCCAGGCCGGTCAGGGTGCCCTTCCAGTCCACGCCGCTGTGGTCGGCGAACCAGCTTATCTTCAAT
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GATCGTGTTGCCCTTCGCGTCGACCATCGTCGATACCGCAGGCACCTTCCCCCTCGAGCAGCTGGGCCGAGCCGTTGGC
AACGACCTCAGANGCAGGATTGGACATCAGCCCTAGCCCGCCTGCGAACGGGAACGTCAGCGCAGTGGCGACGACACT
GGCCAACAGACAGCAGCCAGCCAGCTTCAGAACGGTGATCGCGGCCGGGAAGCGCTCGGGCATGCGTNCCTACAGTAGC
GACCTCCTGTCACTCCACGTGCCGCTCGGTCCAATAGAATCTTTCGCGGGCGGGTGAATCTCTGCNGGATCGGGGCN
GGCGC

::::::::::Rv87T7.seq::::::::::

GCTCGTTGCCGGCGGCGATCTCGTCGAGCTCGTCTTCCATCGCCGCGGTGAAGTCGTAGTCGACGAGCCGACCGAAAT
GCTGCTCGAGCAGACCGGTTACCGCGAACGCCACCCATGACGGCACCAGTGCACTGCCCTTCTTGTGCACGTNGCCGC
GATCCTGGATGGTCTTGATGATCGACGANTAGGTGACGGGCGGCCGATGCCAGCTCCTCGAGCGCTTTGACCAGCG
ACGCCTCNGTGTTNCGGGCCGGCGGGTTGGTGGCATGGCCGTCTGGGGTCAACTCGACNATGTCCAACCGTTGACCCG
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Clone Rv88

::::::::::Rv88SP6.seq::::::::::

GTCTTTGATGGCTGCTTCTTCGGCGCTGACGCTGGCGATCTATCACCCCCAGCAGTTCGTCTACGCGGGAGCGATGT
CGGGCCTGTTGGACCCCTCCCAGGCGATGGGTCCCACCCTGATCGGCCTGGCGATGGGTGACGCTGGCGGCTACAAGG
CCTCCGACATGTGGGGCCCGAAGGAGGACCCGGCGTGGCAGCGCAACGACCCGCTGTGAACGTCNGGAANCTGATCG
CCAACNACACCCNCGTCTGGGTGTACTGCGGCAACNGCAAGCCGTGCGATCTGGGTGGCAACAACCTGCCGGCCAAGT
TCCTCGAGGGCTTCGTGCGGACCATCAACATCAAGTTCGAAGACGCCTACAACGCCNGTGGCGGCCACAACCGCGTGT
TCGACTTCCCCG

::::::::::Rv88T7.seq::::::::::

GCCAGGTGAGGTCCCATGCGCGTGGGCCATTGATGCTGATCGCCAGGACGTCAAANATTTGGTCCGGCGTCAGCTGG
GCGAAAAACGTGGGGCCCAGGACTTGCCCGGAGCTGCCCGGGTTCCCGTCGCGCAGCTCGGCGGGCCCCGGTCAGAAAN
AAATTGCGCCAGGTGCGCACTCCGCGCCGTANGCCAGCTGCTCCAGGGTGTGCGCATAGAGCCCGCGGGCCGACGCG
TGCTCGCTGTGCGCGAACCCGCATGGTCGAGAAGCGTTGCCGCCCAACGGAATCACCTGCGTCNAANGCTTCGCGG
GCCAACTCCAGCACTCGGTGATG

Clone Rv89

::::::::::Rv89SP6.seq::::::::::

NAAACGTTCCGGCTTNGGTGCCGGGCGCTTATTTGCGTCTCTGGGATCACNCTCAGTCGCCGGGCGGCTGCCGTTGGGC
TATNANTTGCACCGANCCGAAAAATCCGCACNANAACCTGCNAGTAGCGGCCTGCAGAANTGCATCCTCGGCGAANNC
ACTACCGGTGGACANCNACAAGCGCCGCCGAACAACGCACTGGCCCGAGGGATNGGCGTCTATCGGGCCCCGCGCGTGC
AACTNGGAACAGACNGTGCGGTTCTACCGTGATCTGGTGGGAATGCTCNACCANACCTTCCCNANNGCTACGGAACNA
CGGCGCGATATTNGCCNTCCCANCTCGAGCCTGACNCTNGATATCGTCGANNCTCACCATCNCGATCNGCTGTGCCG
GTNTTGCTCGGACTN

::::::::::Rv89T7.seq::::::::::

CGAACGACGAACNCCNAAGCCATGGTGGTTGGCGCCGTCAAAGGTCCGCGGTGCCACTACTGGAAATCGCCTTG
AGCGTCNCTCGACNCCGCCTCGAGTTGGGTGNTAACGAAATACCTGATGCCGATCANGTCNACGTCTCCGTGCGNNC
AACGTGACGCGGCGACCCACTCTACNANGTCTCGGTNCCGCCNCGGCCAGNGCACCACAGTGACNAATCCNTGCGCC
NTCGGGCCNAGCANTCCCGGTGCNACCGNGGTGGGTCCGGCGATGGTNGGGTGTNCTCNNTACNGGAACGCCAGCGCN
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Clone Rv8

.....Rv8SP6D.seq:.....
TTAGGCGTGACGGCCACCGGGGCCACTCCGCACAATCTGTACCCGACCAAGATCTACACCATCGAATACGACGGCGTC
GCCGACTTTCCGCGGTACCCGCTCAACTTTGTGTGCGACCTCAACGCCATTGCCGGC

.....Rv8T7D4.seq:.....
CGTACCCCGATGCGCCAGATCGGGGCTTCGCAGATAAAGCACGAACTGGCGGGCAAAACGTCGATCTCGGAGCCGG
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Clone Rv90

.....Rv90SP6.seq:.....
CTTTTCNCGATGTCTCATGATNCCNANGGAGAACNNTGCNANCNCNGCCGCTGACNTNGCNCACCGCTNTGGCNGNGG
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NACCGCANNCCCNATCTCNGCCGCNCCCGGTGGANCTACNGCTNCTTCGCCATCTCTCGCCNATGGCTCCNGCGNNTC
GCNCAACGTNTGGTTTGGTNANCTGCCTACCTGGTCNT

.....Rv90T7.seq:.....
GCTGCGCCAGTCGTTCCGTTGCGGTTCATGCCGTTGGACCNACCATCGGAGTTAGTTGCCGAACCGCGGACCACCGCAAG
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ATCCGCGTTGGCGTCNAANCTGTNGCATCGGTGCGTGGTACAGCGCCGACCACTTGGACAGCGCGATGGCGGTGAA
CGGTNANTAGGTGACCTGCCNCCNCGCCGCCAATGCCACCTCCGCTTACNCATGCGAATGGTCTGACACGCCNAG
TGAATTGCCACCAGCGACAACAAAATCGGTATCTNCNGCGACGGCGGACACGCNATCCCNACTGATACTCGATCCGC
CCCACCGCTTGNANCTCCGGGTTCCNGTGCTCATGTACNCTCATGTGGTCTGCGCNCGATATTGACGATCGTGTTTC
CCACGANNANAGANCCATCACGCCGGTTCGAGTGCCG

Clone Rv91

.....Rv91SP6.seq:.....
CTGTGTGCGGNCGGCGGATATCGGCCTTTTTACTAACCGAACCCGATGTGGGCTCCGATCCGGCGCGCATGGCATCT
ACNGCGACGCCGATCGATGACGGCCAGGCTTACGAGCTTGAGGGTGTGAANTTGTGGACCNCCAACGGTGTGGTAGCG
GACCTGCTANTGGTTATGGCGCGGGTACCGCGCAGTGAANGGCACCGAGGGGGAATCANCGCCTTTGTCTGTCTANGCT
GATTCTCCCGGGATCACNTGGAGCGCNCNCNANTTCATGGGACTGCGTGGCATCCAANACGGCGTGACCGGCTTCA
TCCNTCNGGGTGCCCAAAGACAACCTTGATCNGCNGGAAGCGACGTCTGAANATCGCGCTGATCNCACCTCAACGCCGG
ACGCTGTCTTACCGGCGATCGCACCGGANTTGCCAANCCGCGCTNANNATNCGCGNGAATGNCCGTCCACNANTGCAT
GG

.....Rv91T7.seq:.....
TGGGGTGCCGGGCGCCGAGTTGCGTCCCTGGGATCACGCAGAGTCGCCGGCGGCTGCCGTTGGGCTATGAATTGCACC
GAGCCGGAATAATCCGCANCAAACTGCGAGTAGCGGCCTGCAGAAGTGCANCCTCGGCGAAACGGAGTACGGTGGACA
ACGAAAAGCGCCGCCGAACNACGCACTGGCCCCGAGGGATTGGCGTCAATCGGCCCCGCGCTCGAACTTGGGAAGANAC
ANTGCGGTTCTACCGTGATCTGGTGGGAATGCTCCAACNNACCTTCNCCGAAAGCTACGGAAGCNACGGCGCGATNTT
CGGCCCTCCAGCTCGACCTGACGCTGGAAATCG

Clone Rv92

.....Rv92SP6.seq:.....
NGGCNGGGAAGTTAATGCCCTACTGGTTCNATGCTCNCACNTCNCNGTGACNNCTGCNCCGACCCGCCGAGGTCTT
GNCCGTNACCACCGANCNCGCGATCCGGGACTCTNGTACGCATCCAACANNGANCAACGTGCACGGGCGGAGTNGTNC
CGCCACTTCGNCNATGACGGGTGCGATCCNTTCGACGTCCGTGCGCGCGTGGTTCGAGTGGCGGTACNCTCCNNGTA
CTCGACCNCACNACGAGAGGACTCGANCCCATCTACGTGTGGACGAAACANATCTTCTGTCNACGACTACACCACC
ACCCAGGCCATCGCCGNCGCCGCGGANGCCCTTCGACGCCNTACTGGTCCNGNGGNGGCGCTCTCCGGTTGTCTNNC
NCNTGNCGTGTTCTTCACNCACTGCCCNACATCGANCCCGAGCNATNCNANGTCCGTCAATC

.....Rv92T7.seq:.....
GGACACTGTTGCGGTGCCCTCTGTCAAAGCCGGAGTGGTCTGTGCTGCGCCGACCCGACCCGACCTTCAGCGGGGGTT
CACAGCTCCGTGGGTGCCGTTACTTCCGATCGCCGAGTGTGCGCGTGCTGTGGCTGATGCTGAACCTCACCGCGTT
GACTTGGATCCGGTTCGGGATCTGGCTGGTGGCCGGAACCGCGATTTATGTCNGCTACGGGCGCCGGCACTCGGCGCA
TGGCCTTCGGCAAGCNCNANANAACGCGACCCGGAGGTGTTGAACTAGCTTCGCCGCGTATTTACAAATTGCNTTATA
TGTCTACACATAAGACGCAAACTGCTCTATTGTCAANTCCCANCGTGGTGTGGCNCATGAAGATGTTTGG

Clone Rv94

:::Rv94SP6.seq:::

TCCTTCTCGGTATCGGTTTGGGCTGTACCANCAGTTGGTAGTTCTTCACGTNCTGTTGTTTCGAGCGTCNAGCCGTCG
CGCGTGTNCANGTCNCCGGACGCGTATCCCGCCAGGCCGGTCANGGTGCCCTTCCANTCCACGCCGCTGTGGTTCGGCG
AACGCTNATCTTCAATCGAGACCATCGCCAGCTTCATCNTGTTGGCGATCTTGTTCNNACGGCACCTCNAACCGGCGCT
NCTAGTACNCCACNCNATCNTGTTNCCTTCNCGTCNACATCCTCGATNCCNCNTGCACCTTCCCTCGANCNCCTGGGC
CGAGCCGTTGGCANTNACCTCNGAGCCCCATTGGACATCANCCCANCCCGCTGCCAACGGGAACGTGAGCNCNCTGG
CGACAACCTGGCCAACAN

:::Rv94T7.seq:::

CACNCCGTGATCGCNAGCCCCNGTAGAAATNGTTGAGCCAGTTGGTGCGGCGCTCGTTGCCGGCGGTTNATCTCGTCGA
GCTCNTCTTCCATCGCCGCGGTGAAGTCGTAAGTCGACTCGACNAGCCGACCNAATGCTGCTCNAGCAGACCGGTTACCNNA
ACNCCNCCTCNTGACNGCACCAGTGCNCTGCCCTTCTTGTGCACGTACCCGCNATCCTGGATGGTCTTGATGATCNAC
TANTNTGTCGACGGGCGGCCGATGCCATCTCCTCNAGCGCTTGACCAGCGACNCTCGGTGTATCGGGCCGGCGGG
TTNGTGGCATGGCCGTCTGGGGTCANCTCNACNATNTTCANCCGTTGACCCGGGGTCACA

Clone Rv95

:::Rv95SP6.seq:::

TGGCCTTCTTGNCANGGGCANNACATNNGCTATNGCGAGCGTGTAACCGATCATCNTCCNGGCGACTGTGGCCTGANCG
GCAAGGGTNGCCTNATTCNTCCTCCTGNGGCATGGTTNCCACACGGAATGNCGGTAAGTCTGGTCGGCAACCTGGCCC
GCTGCGGGTTGGGTTTCGGATTTCGCTCGGCTANTAAGGTGCTCGCCTGGTGTNACNACTAATCNCNATATACNCTTANC
GGGAGTNGNCGTCCCGATCCTNGCCCTGCCGCNNGCGATCNCGTTTCGCANACCCGCCACCGGAACCTCNCAANGTGC GC
TCATCGGGCTCTACGCGCCATCTTCCCGGATTCTTCGCGGCNNGTNCCGNGGGACCCCGGACTGTGACNGGCCCAA
CGGCTCATCATCG

:::Rv95T7.seq:::

CCGGATAGCGGTGTCTGAACCTTCGCCCGTTCCCTCANCGCATTGAGCTTCAGCCCCAGCGGAGGTNNGGAGTCGGC
ATGCGGTCTTCGCCCGACCCCGCTGGCTAAATANCCACCCCGAGCGCGGTACCGGTCTTTGCACCGGGACGACGC
ATACCGGCAGCGCAACATCNCGCGGGCTGCAGCNTGAACGTCCAATACCANTCNAACAGTGTCCGCGCGTNAACAC
CCGANCCGGCGGTTCGCTTCNGTAATCAACGGCTCCTGCGCAACCAGCTGCAAGTCGCCGGTGCCACCGGCGTTGACGA
TCTTGATGTCTGCGANCTCGCGCACCAGCTCGACGGCCCGGGCA

Clone Rv96

:::Rv96SP6.seq:::

CCTCCCGACCACATACAGGCAAAGTAATGGCATTACCGCGAGCCATTACTCCTACGCGCGCAATTAACGAATCCACCA
TCGGGGCAGCTGGTGTGATAACGAAGTATCTTCAACCGGTTGAGTATTGAGCGTATGTTTGGGAATAACAGGCGCAC
GCTTCATTATCTAATCTCCAGCGTGGTTTAATCAGACGATCGAAAATTTCAATTGCAGACAGGTTCCCAAATAGAAAG
AGCATTTCTCCAGGCACCAAGTTGAAGAGCGTTGATCAATGGCCTGTTCAAAAACAGTTCTCATCCGGATCTGACCTTT
ACCAACTTCATCCGTTTCACGTACAACATTTTTAGAACCATGCTTCCCGAGGCATCCCGAATTTGCTCCTCCATCCA
CGGGGACTGAGAGCCATTACTATTGCTGTATTTGGTAAGCAAAATACGT

Clone Rv9

:::Rv9SP6.seq:::

CTTCACNTCCGTACGGCTCGGGTACGCTTCGGTCNCATTGTGCGAGTGATAGATGACGACCGGGACCTCGTCGGCATC
TTCCATAGCCCCGCCACACCTTCAGTTGCTCACCGGAATCCAACCGGTANAAGGTCGGCGANCGCTCNGCATTGGTCAT
CGGGATATGCCGCTCGGGACGGTCANAGCCCTCGGGTCCGGCCAGCACTCCGCGAGGCTTCGTCCGGGTGGTTCGCGACG
CGCATGGGCCACCATCGCATTCACCAGGTCTGCGCGAATCACCAGCACGTANACGGTTCCTTTCCCTAAGCAACACCGA
ANTTTAGGACCCGAATGCTCCGGGAAACATGTCACGGTAGGTGCGTATTCCGGCTACCGGCTGANCATTGAGCACGC
CGGCCAGCACCGCACGAACCAGGCAATCAGCCGCCGCCGACCCGACCGCGG

:::Rv9T7.seq:::

CAGGCATGCAAGCTTGATGCCGCCGAAACCGAGCGTGAGCACGCCGCCAGCCACCACGCGCGGGTCGGGCGCCGGGCC
CGGGCCGCCAGGCTGCTCCGCTCGGTGATGGCACGCCACCGCGACACCACCGGCTGCGCTACGTCGAGCCATACCGG
GCGGAGCTACATCGGCTCGGCCGCCAGTGTTCCGGGCCCTCTTTCGAGGTGAGGTGATACCGATTTGCGCATCCGC
AGCCGCACCCTGGACGACAGAACCCTGACGAATTGCTTGTGCGGGCGGGGCCAAAGAACAGCTTGGCATCCTGGC
GCGATTGGCCGGCGCGGCGCTGGTCGCAAGGAAGACCCGTTCCGGTGCTGAT

Table 4 : End-sequences of the polynucleotide inserts cloned in the named recombinant BAC vectors contained in the I-XXXX *M. bovis* strain Pasteur genomic DNA library.

RvXXXSP6 corresponds to the SP6 end-sequence of the clone RvXXX.

RvXXXT7 corresponds to the T7 end-sequence of the clone RvXXX.

RvXXXIS 1081 corresponds to a region located close to a copy of the IS1081 repetitive sequence (Insertion element).

The character « - » denotes an uncertain base residue.

Clone X0001

.....X0001SP6.seq.....

AAG-

TCGGGTTTCCACACGCGCGGTTTGACCCTAGTCATATGTAATCATGTGTACCATGTGCGGGCGCTTTTCGACGGCCG
CGAACCACCGGA-ATTTCTGTGATTTCACCTGCATGCGTACCATCTGGCACAATTGAGCA-TTGTCT-
TCGCGGTGGTCGG-CGGGTGCGTGCCGCCTGCTGCGA-ATGCACCA-
TAAGCCCGAACCCACCGGCTTGGTGACCACCGCACGCTGCGTGTGGGGGGTAACCACTCCGCGACCCCAAGGATGGT
CATTTCCAATGAACCGGCTGGACTTCGTCCA-A

.....X0001T7.seq.....

GTCGCGGTTTCGATCGACCGATCTTCACCTCGTAACCTCGATGCTTAGCAGGATCCAGCTTGACCGCGTTTGGCTCT
ACCCACTCTTTGAGTGGCGCCGTCGCTGTGCCCCATCGGTGTTTCATGACGAACGCTTCGAAAGACTTCCTCTTGTG
AGCCGGAATGTCTGCGTAAAGAAGTTCATGTCCGGGAAGTAGACCCGGTCGCCCTCCACGTGGTACTCCTTCGAGG
TCCGCTTCTCGCCGGATCCGATAAACACCGGCCCCAGGCACCGCAGCGTGAGTTCGAACGGCTTCAGGTAGGTGTTT
ATCGGCGGACTCCGGGAGTGCAGAGAAATAGCGGTGCGCGGTAGCTGTAGACCGGATGGTTTCCGCCCAGGCTGACG
TCGAAGATGCCTCCTTGAAGGGGCGCGA

Clone X0002

.....X0002SP6.seq.....

AACTCAAGTTTTTACGGTGATCGCGCATCACCTGGTTCATGAAGTGAAGCAGCGCAGCGCTTCCTTTTCGGCCGCA
ACATGAGCCAGCCTCTCGTCGGCGGTGCGGTGTCAGGTGCTCGGGCAGCTCGGCCGCGACAGCCGCCTGACCTGAAA
CCAGCTTCCATATCCCGCGAC-
AACGACGCCAGTCCGCTACGTAACCCCTCCGCGACTGTCCATGGACAACAGCGGTTCTCCACCGACCGGGCCCGGG
TGT

.....X0002T7.seq.....

GTGCAGGTTTCGACAATGTGGTGCCGGTTCGGCGGCTACGTGCCATCGAGACACTGGCGCA-GCTATCGCACCCGTT
ATCGGCTGCGAGCAAATCGCGGTATGCGTTCTTGAGCATGAGTCGGCGACCGTCGTCATGGTCGACACCCACGACGG
AAAGACGCAGATCGCCGTCAAGCATGTGTGCCGCGGATTATCAGGACTGACCTCCTGGCTGACCGGCATGTTTGGTC
GCGATGCCTGGCGCCCGCGCGGTGGTCGTGGTTCGGCTCGGATAGCGAGGTGAGCGAATTCTCGTGGCAGCTCGAA
AGGGTCCTGCCGGTGCCGT

Clone X0003

.....X0003SP6.seq.....

TTCGAGTCATGCGCCCGCCTCGACCACGAA-ATGCACGTCG-
GGTTCGATCGACCCGATCTTCACCTCGTAACCTCGATGCTTAGCAGGATCCAGCTTGACCGCGTTTGGCTCTACCCA
CTCTTTGAGTGGCGCCGTCGCTGTGCCCCATCGGTGTTTCATGACGAACGCTTCGAAAGACTTCCTCTTGTGAGCCG
GAATGTCTGCGTAAAGAAGTTCATGTCCGGGAAGTAGACCCGGTCGCCCTCCACGTGGTACTCCTTCGAGGTCCG
TTCTC

.....X0003T7.seq:.....
GTCATGTGTACCATTTGCGGGCGCTTTTCGACGGCCGCGAAACACCGGAGATTTCTGTGATTTCACTGCATGCGTA
CCGTCTGGCACAATTGAGCAGTTGTCTGTCGCGGTGGTCGGCCGGGTTGCGTGCCGCCTGCTGCGAGATGCACCAAT
AAGCCCGAACCCACCGGCTTGGTGACCACCGCACGCTGCGTGTGGGGGTAACCACGCCGCGACCCCAAGGATGGTC
ATTTCCAATGAACCGGCTGGACTTC-TCAACAA

Clone X0004

.....X0004T7.seq:.....
AACAGCGCGGTTGAACTGATAGGTGCGGCCCGGCTCGAGCAGGCCGGGCCATTTGTTTCGATGCGGTTACCGAAAGAT
CTCTTCGGTGACCTGCCCGCCGCCGGCCAGCTCGGCCAGTGCCCGGCGTTGGCCGCCGCGGCGACGATCTTGCGCT
CCACGGTGGTCGGGG

Clone X0006

.....X0006T7.seq:.....
GCATCTGGGCTGGCGGTGGTTTCGCCGCTCCGAAGCCGTCGAACACCATCGCCAGCGGGCTTCCACATCAACGACCA
TTTCGGCCAGCTTGCGGCGCATCAGCGGCTTGTGATGAGCGCCCCACCGAATGCCCGCCGCTGCCCGGCGTA-
CACAGCGATTCGACCAGCGCGCGCGCGCTTGCCGAGGGCGAACGAAGCGGTGCCCAACCGCAATCTGTTGGTCAG
CTCCATCATGCGGGTGAGTCCCTTGCCG

Clone X0007

.....X0007SP6.seq:.....
ATCGGTTTCAGCAACAGCCGATCGACGGCTTCGCCCCA-
GGCCGCTCCCGGGCGACCCGACCATTTGCTGTGCGCCGCGTAACGCCATCACGGATGACGCGCAGTTCGTGCTGTCTA
GCTCCACCATCGCCTGCACACCGGCGGCCAG-ACCCATTGGCCGTCGCACTCGTA-
AGCAGGTAATCCTCGTCGACGGACTCGGTAACACCGCCGCGCAGCTCCGCTGCCAGGTGCGCGGGGTTGACACCGGC
GGGCATCGGGATGGACGACGACGCGGTGCTGACGGCGCCTGTC

.....X0007T7.seq:.....

AGCGGTTTCCCA-
GCGGGATGTGCTGTGAGCGCCGACACCAGCGCCGACGCTAAGGATGGAACGCACGGCATCTTCTGACGCGTAACC
GCGTTGTGATCGCGAGCTGAGGAGACGGTATGGGGGAGGGTTCTCGGAGGCCATCTGGGATGTTGATGTCTGTCGAT
CTTGAGCCGGTGCAACTCGTCGGCCCGGACGGTACGCCGACGGCCGAACGCCGCTACCACCGTGACCTTCCTGAGGA
AACGCTGCGTTGGCTCTACGAGATGATGGTGGTCACCCGCGAGCTGGATAACGAATTCGTCAATCTGCACG

Clone X0008

.....X0008SP6.seq:.....
CAAGCTTCCACAGGTAGGGATCGAGGAACAGCGCGTTGAACTGATAGGTGCGGCCCGGCTCGAGCAGGCCGGCCATT
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CGCCGCGGCAACGATCTTGCGCTCCACGGTGGTCGGGGTCATGCCCGCAGCAGGATCGGCGAGCGGCCGGTCAGCC
GGGTGAACTTCGTCGAAAGCTTGACCCTGCCGTGCGGGAGGCGAACCACGGTCGGTGCGTANCTCCACCAAGCCCGG
GCAACCTCGGGGGTGCGCC

.....X0008T7.seq:.....

TGGACCTCATGACAACGCGGCGGCGATTACCCCGCTACCGCCAGCAGCATGACGGCGGTAGCGAACACCGCCGGAT
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AGCGCGACACCGACGATTCGGTACACCGCCACGCCGATCAGGCCCTGGGCCAGCTGGCGTATATGGCGGCGATGGTG
ACGATGGCCAGCGCCACATACATTGTGGCGGCCAGAACCACGGCGTTGGGGCGGCGGTGATGAACACTAGGCGACG
CAGATCGCCCGGGTCAACAGGTTGACCATCAGAAAGCCTGCGA

Clone X0009

.....X0009SP6.seq:.....

TTTGGTGCGGCCGGCAATCAACTTC-GCTC-
CAGCGGTTTCCAGGCGGGATGTGCTGTGAGCGCCGACACCAGCGCCGACGCTAAGGATGGAACGCACGGCATCT
TCTGACGCGTAACCGGTTGTGATCGCGAGCTGAGGAGACGGTATGGGGGAGGGTTCTCGGAGGCCATCTGGGATGT
TGATGTCTGTGATCTTGAGCCCGTGCAACTCGTCGGCCCGACGGTACGCCGACGGCCGAACGCCGCTACCACCGT
GACCTTCCTGAGGAAACGCTGCGTTGGCTCTACGATATGATGGTGGTCACCCG

.....:X0009T7.seq:.....
CGCCAGGGCCGCTCCCGGGCGACCCGACCATTGCTGTGCGCCGCGTAACGCCATCACGGATGACGCGCAGTTCGTCCG
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GTCGACGGACTCGGTAACCACCGCCGCCAGCTCCGCTGCCAGGTGCGCGGGGTTGACACCGGCGGGCATCGGGATGG
ACGACGACGCGGTGCTGACGGCGCCTGTCGCGACGCTGAGCTCGGACACAGCTAGTAAATGTAGCCTAACCTACTTA
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GCACC

Clone X0010

.....:X0010SP6.seq:.....
AATACTCAATCTTGATCGGTTTCCAGCAACAGCCGATCGACGGCTTCGCCAGGGCCGCTCCCGGGCGACCCGACCA
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CGGCCAGGACCCATTGGCCGTGCGACTCGTAGAGCAGGTAATCCTCGTCGACGGACTCGGTAACCACCGCCGCCAGC
TCCGCTGCCAGGTGCGCGGGGTTGACACCGGCGGGCATCGGGATGGACGACGACGCGGTGCTGACGGCGCCTGTCGC
GACTCTGAGCTCGG

.....:X0010T7.seq:.....
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GAGCCGGTGCAACTCGTCGGCCCGGACGGTACGCCGACGGCCGAACGCCGCTACCACCGTGACCTTCTGAGGAAAC
GCTGCGTTGGCTCTACGAGATGATGGTGGTCACCCGCGAGCTGGATACCGAATTCGTCAATCTGCAGCGCCAGGGGG
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CTGGTTGTTCCCC

Clone X0012

.....:X0012SP6.seq:.....
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GAGGCCGGCTGGGAC-
CCGAGGTGGCTCGTCGGCCACATGGGCAGCACACCACCGTGGTGATGCATCTAGACGTGCAGGACCGTGCCGCTGGC
CTGCA

.....:X0012T7.seq:.....
GCGGCTACGTGCCATCGAGACACTGGCGCAGGCTATCGCACCCGTTATCGGCTGCGAGCAAATCGCGGTATGCGTTC
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Clone X00013

.....:X0013T7.seq:.....
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CGAACCCCGGATGCTGCTGGTCCATTTTCTCCGTGATCAGCTGCGGCTCACCGGAACCTACTGGGGCTGTGATACCA
GCAACTGCGGGACATGCGTGTTGGAGGTCGACGGCGTGCCGGTGAAATCCTGCACGATGCTCGCCGTGATGGCCTCC
GGG

Clone X0014

.....:X0014T7.seq:.....
AGCGGCTGGTTACGACTCCCTGTTGTGATGGACCACTTCTACCAACTGCCCATGTTGGGGACGCCCCG-CC-
TCCGATGCTGGAAGCCTACACTGCCCTTGGTGCGCTGGCC-C-GCGACCGAGCGGCTGCAACTGGGCGC-
TTGGTGACC-GCAATACCTACCGCACCCC-ACCCTGCTGG-CAAA-
ATCATACCACGCTCGACTTGGTTAGCGCCGGTCTGA-CGATCCTCGGCATTGGAACCGGTTGGTTT-

Clone X0015

.....:X0015SP6.seq:.....
ACGCGCGCCGATCATATCTGCTATGGATGTACAATTACGCTCTTGCTGTTATACCAGTATATGGTGTACTATTTGAT
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ATTCTGGTGGCGTTGCTGGATGGCGTTTGTCTATCCCGCCAGCTAGCTGCGCACCTCGGGTTGACCCGATCGAATGT
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.....X0015T7.seq:.....
CCGCGCTGCTGCTGACGTCGGTCGAACGTGCGACACGTCTGCGAATACCGGCCGAACGCTGGGTTTATCCACAGGCT
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TGCCCGGGCGCTGGAACCTGGCTGGGCTGGGGCTCGATGACATCGAATACGTTCGACCTGTATTTCGTGCTTTCCCTCCG
CTGTCCAAGTCGCCGCAATCGAACTCGGCCTGGACACCGACGATCCTGCCCGCCCGCTGACCGTTCACCGGGGGCCCTG
ACCTTCGCCGGCGGGCCGCTGGAGCAATTACGTTCACGCACTCCAT

Clone X0016

.....X0016SP6.seq:.....
CAGGCGTGCAATGACCTGCACTGCGCCGGA-A-
TCCCTAACCCTAAACCGGGGCCGCTCACAAGCCGTGCAGCTCGGTTCAGGTTCAGGTGCGCGACCCAGGAA-
TAAATGAGCAGACCCGTGCCGTCAACGATGGTGGCGATCATCGGCCCGGAAACGATGGCCGGGTC-
ATGCGCAACTTCTTCAGCAGCGGCGGAAGGACGGCA-CCACCAGCGAC-ACCACACCACGAT

.....X0016T7.seq:.....

GCGAA-
CACTTCGTCAACTTCCAGGGCTGCCCCGACCAAGTATTTTCGACGAGTATTTCCGTGCGGGCCGCCGCCGCCGGCGCGC
GGCAGGTGGTCATCCTGGCGGCGGGGCTGGACTCGCGCGCGTACCGGCTGCCTTGGCCCGACGGGACCACGGTTTTT
GAGCTGGACCGCCCGCAGGTCCTTGATTTCAAGCGCGAGGTGCTCGCCAGCCACGGTGCCCAACCGCGCGCCCTGCG
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CGGCATGGATTGCCGAAGGGCT

Clone X0017

.....X0017SP6.seq:.....
TTGGGC-TTGCCC-CAATA-GGCCCCAATCAAAAGCCGAGCAGGTGGAACCTA-CGCATTTCGCCTC-TCGT-
TGTGCACCCGAGCCATCGCACGCGCGGGAATTCCCGGAT-TC-
CCGTATTCTCCGGCGGCCGGGCTAACCCTATCCCA-GCCGAACGGTTGGCTC-
TGCCGTGGGTCCCCTGTTGGCCGATCGGGGCGTCACCGGGGGTGCTCGGGTGCGG-TGACCATGGC-AACTGCCCC-
ATGGGCCGACCCCTGGTGCAGATAAACCTG

.....X0017T7.seq:.....

TGGTGAGGTCCCCACCAA-ACCGGCCGTAACCTCTGCTCACGGAAATGCGG-
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GTGGAAGGTGCCGTGCGCGAAGATCCCGGCGTTGCTCACCACACCGTGCACGGCGCCGAATTCGTCAAGCGCGGTCT
TGATGATGTTTCGTGCGCCGTCTCGGTGGCGACGCTGTGCGTA-
TTGGCGACCGCCCGGCCCCCTTGTGCGGAAATCTCGGCGACGACCTCATCGGCCATCGCCGAACCGGGCGCCCC

Clone X0018

.....X0018SP6.seq:.....
GCCGGCCAACTGGCCGGCGGGGTTGCTGTC-TCAAGGTGGGTTCGCCACCAA-ACC-
CACTCAAGGATCGCAAGGAAAGC-
TCAAGGATGCGGTGCGGGCCGCCAAGGCCGCGGTCAAGGAGGGCATCGTCCCTGGTGGGGGA-
CCTCCCTCATCCACAGGCCCGCAAGCGCTGACCGAAGTGC-TGCGTC-C-GACCGGTGACAA-
GTCCTCGGTGTCCACGTGT-CTCCGAAGCCCTTGCCGCTCCGTTGTTCTGGATC-CC-CCAAC-
CTGGCTTGACGGCTC-GTGGTGGTCAACAAGGTGAGCGAGCTACCGCCGGGCATGGGCTGAACGTGA

Clone X0018

.....X0018T7.seq:.....
CGAACCT-AATTGTCCTGTAATGCCAGCTCACCAA-
GCATGGCTGGTGGCCGGGGCGGTGAAGCCGGCGTCTGCGGCACCGTCCAATC-ATGTGGAT-
GCCGGAATGGGGATGTCCGG-ACGGCGAATCCGTA-
TTCGCTTGTCCCGTGAGGCCAGGTGGATGGGGGGAAGGATC-TGGTGTCCGGGATGAT-
ATGGGGCCGATGCCGCCGTTGAAGTCCACTGGATCGGGAATTCGGGAATCGTGAT-CCGACGTTTCAGGCCGAAC

Clone X0019

:::X0019SP6.seq:::

CTAACGGAATGAAAGCCCTGGTGGCCGT-
TCGGCGGTGGCCGTCGTCGCACTGCTCGGTGTATCTTCCGCCCAAGCTGATCCCGAGGCGGATCCCGGCGCAGGTGA
GGCCAACTATGGTGGCCCCCAAGTTCCCCACGTCTTGTGATCACACCGAATGGGCGCA-
TGGGGAATTCTGCCAGCCTCCGGGTCTACCCGTCCCAAGTTGGGCGTACA-
CCTCCCGCCGCTCGGGATGGCCGCTGCCGACCCGGCCTGGGCC-
AGGTTCTCGCGCTGTCAACGGAAGCCGACACTGCCGGC

:::X0019T7.seq:::

CCGCGGGACAC-CCTC-
ATGCTGCCGCCATGGACGCGGTCTGAACGCAAGCAGCTGATCGAGCTACAACGCCGCGCGGAACGCTTCCGCCGCGGG
CGTGACCCGATCCCGTTGACCGGGCGGATCGCGGTGATCGTCGATGACGGCATCGCCACCGGAGCGACGGCCAAGGC
GGCGTGCCAGGTGCGCCGGGCGCACGGTGCGGACAAGGTGGTGTGCTGGCGGTCCCGATCGGCCCA-
ACGACATCGTGGCGAAGATTGCGCCGGGTACGCCGATGATGTGGTGTGTTTGGCGACGCCGGCGTTGT

Clone X0020

:::X0020T7.seq:::

CTCTGGGACCGGCCACGGTGCC-
CCGGCGTTCCCGGACGTGCTGCGCCAGGTGTCCGGCGGCCGCGTGCATGGTGTTCCTCGGATCGGCCGCTGGCCAGAG
CCCACCGGTGAATCTGGCGCCTGGCCGACCACCGTGCGCCGTAGGCTTGGCATCGTGCAGCGCTGGCGTGGCCAGGA
CGAGATCCCGACGGATTGGGGCAGATCGCTGCTCACCATCGGGGTATTTGACGGCGTGCACCGCGGGCACGCCGAAC
TGATCGCGCACGCGGTCAAAGGCGGC

Clone X0021

:::X0021SP6.seq:::

AATACTCAAGCTTTTCGTCACTTCATTGCGCCAGCAGACCAACAA-AGCATCGGGACATACGGA-
TCAACTACCCGGCCAACGGTGATTTCTTGGCCGCGCTGACGGCGCGAACGACGCCAGCGACCAC-
TTCAGCAAATGGCCA-CGCGTGCCGGGCCACGAGGTTGGTGTCTCGGCGGCTACTCCCAGGGTGCGGCCGTGATC-
ACATC-TCACCGCCGACCACTGCCCGGCCTCGGGTTACGCAGCCGTTGCCGCCCGCAGCGGAC-
ATCACATCGCCGCGATCGCCCTGTTCCGGAATCCCTC-GGCCGCGCTGGCGGGCTGATTAAC

:::X0021T7.seq:::

TGCCGCGGATTTGGCTGGCTGCCCAATATTGAGAATCGGGCCTTTCTTTTGGCGGACAATAAGGTCACAGTAAACC
CTCGTTTTGTGAGATGCGGGGCGGGCCGGGCGAA-
TCGACCTCGAGTGAATGGATCTCGAGTGAATGGACAGGGCATCGCCTACGAGTCGCATCCCCATCCAACAGACCGGT
GCTCTTGATCGGACCCCTGAAGGTCCCGCACGGAGGGTGTGGTTGCCGGCGCGGGGTACCGGTGCGGTAGCGACGTA
GTGTTTGAACGAATTTCTTGATGCTCCAACCTGTTTGGTGTTCATCCAGTTCT

Clone X0175

.....X0175SP6.....

AA-CTTGCGCGCTCGGCCGGGTC-AGCATCCAGCTGCTCGGCAAGGAGGCCAGCTAC-C-
TCGCTGCGTATGCCCAGCGGTGAGATCCGCCGGGTC-
ACGTCCGCTGCCGCGCGACCGTCGGCGAAGTGGGCAATGCCGAGCAGGCAAACATCAACTGGGGCAAGGCCGTCGG
ATGCGGTGGAAGGGCAAGCGCCCGTCGGTCCGGGGCGTGGTGAT-AACCCGGTC-
ACCACCCGCACGGCGGTGGTGAGGGTAAACCTCCGGCGGCCGTACCCCGTTAGCCCGTGGGGCAA

.....X0175T7.....

A-TCGAAAGTGACCATCTTACCTTGAGTGCCATACCGCCCGACCCTATGCCTCGGATAGCTCGGCGGAAAGAAACG
CTTGCACTGCCCGCAATAGGCGGCTACGTGCTGAGCGCCCATCAACTCTCGCGCGGAGTGATCGCCAGCTGGGCG
GCGCCGACGTGACCGTGGGGATTCCGGTGCGCGCCGCGGCCAACGGCCGATCGTCGACCCGCACGGCAGATCGGC
GCGATGTTGTAACGCTGCATAGGCACTCCCGCGCGCTGGCAGGCCAGTGCGAACGCCGCCGCGGTGCGTCCG

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